Tooth whitening products in toothpastes and mouthwashes may act as co-carcinogens in the oral mucosa

How to advise orthodontic patients and how to avoid undesirable effects

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At the conclusion of clinical orthodontic treatments, patients very often ask about the need or possibility of tooth whitening. During treatment, patients sometimes ask about the use of toothpastes or mouthwashes with whitening products. In several situations, they may ask direct questions, such as:

» Is bleaching good or bad for my health?
» Does it cause cancer?
» Are you in favor or against it?

We discuss tooth whitening in this article as a way to help orthodontists to define indications and establish guidelines for their patients.

Since the old Egyptian civilization, human beings have expressed their desire to have bright, white teeth.[12,41] According to historical references,[22] the pioneering external tooth whitening procedure should be assigned to Atkinson, who, in 1893, described the use of a 3% hydrogen peroxide solution as a mouthwash for children to reduce caries and whiten their teeth. He found that at a 5% concentration, whitening was greater, and much greater when concentration was 25%, but the risk of lesions to soft tissues increased substantially due to the caustic effect of the whitening product. Tooth whitening has been described in the scientific literature since the beginning of modern times.[6,15,20,48]

External tooth whitening became popular in 1989, after Haywood and Heymann[23] published a study that received media attention in the form of articles and commercials. Internal and external whitening products are similar and all have hydrogen peroxide in their composition. They may receive different names according to their composition and presentation: urea peroxide, percarbamide, carbamide, sodium perborate and others. Some of them release or change into hydrogen peroxide only when applied to teeth.

In the search for esthetic results and white, vital teeth, which have a strong commercial and advertising appeal, whitening products have been added to the composition of mouthwashes and toothpastes.[19,29,31,37,39,40] Hydrogen peroxide has often been incorporated into products whose

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primary function is antiseptic.[2,49] Recently, dyes have been added to toothpastes for a passive process of tooth whitening with visible, transient but immediate results.

Products classified as cosmetics should not have any therapeutic function and are not supposed to affect body physiology. In 1991, the Food and Drug Administration (FDA) removed whitening products from the list of cosmetic products and reclassified them as drugs or medicine. In 1994, the American Dental Association (ADA) established criteria and recommendations for their use to ensure efficacy and patient safety.[1,10]

According to the ADA, products with hydrogen peroxide for home use are divided into three groups:

a) Antiseptic products with hydrogen peroxide, whose contents should be known by dentists and patients and which should be used only for short periods of time.
b) Whitening products containing 3% hydrogen peroxide or carbamide peroxide, prescribed by dentists that, together with their patients, should be familiar with their contents.
c) Tooth pastes, that should have low concentrations of hydrogen peroxide or calcium peroxide.

Toothpastes and antiseptic products should be prescribed by healthcare workers, who are primarily responsible for their patients' choices because these products are different from those that patients choose to buy voluntarily, even when they know their risks, such as tobacco and alcoholic beverages.

Hydrogen peroxide is also found in other products, such as coffee, and is present in industrial processes to produce foods, such as fruit juices, because of its antibacterial and antiviral properties.[29] The human metabolism also produces hydrogen peroxide and, for example, stores it in cytoplasmic granules to fight bacteria that the cells, particularly neutrophils, destroy by phagocytosis.

The undesirable effects of whitening products

With a few exceptions, all treatments using drugs might have undesirable effects, and this is also true with whitening products. When directly applied to the dentin, they produce demineralization that results in the enlargement of dentinal tubules because of their acidity when acting upon the dentin. In the cemento-enamel junction, they enlarge exposed dentin gaps found in all human teeth, even primary teeth.[9,13,14,16,17,32]

In general, whitening products are composed of hydrogen peroxide when they act on the tooth surface, although they may be composed of and called something different, such as carbamide peroxide, urea peroxide and sodium perborate. When applied externally, whitening products act as acid solutions and may increase superficial enamel porosity, promote the separation and infiltration of composite restorations, and induce discrete subclinical pulp reactions or dentin hypersensitivity.[9,13,14,16,17,32] However, of all undesirable effects, the ones that stand out are the effects on soft tissues:

1. They "burn" or necrotize soft tissues due to the caustic effect of hydrogen peroxide.
2. They participate as promoters, or co-carcinogens, in chemical carcinogenesis, potentializing the effects initially induced by carcinogenic initiating agents,[3,4,7,8,10,11,18,28,29,33,35,36,38,39,42-47] including those in other points of the gastrointestinal mucosa.

The action of carcinogenic agents on tissues has a cumulative effect along life, and malignant tumors are often found after the fourth decade of life. Along life, the effect of a carcinogenic agent is irregular and unpredictable in most cases, and its actions are invariably added to that of other agents and environmental factors or inherent characteristics of each individual. This is the reason why there are no accurate estimates about the biological and clinical risks for an individual that accumulates exposure to the sun, smokes or consumes alcohol, for example.

The frequency of tooth whitening in current clinical practice and the addition of chemical whitening products to mouthwashes and toothpastes indicate that we should know in detail how they act and what consequence their action has on the oral mucosa. Teeth are brushed several times a day, and knowing what has been added to and used for oral hygiene may help to preserve the oral health of the population and define preventive attitudes.

The effect of tooth whitening products on oral carcinogenesis: promoters but not initiators

A study[33,34] about the carcinogenic effects of whitening products was conducted using a universally accepted and knowingly effective experimental model in which the products were applied to the oral mucosa of hamsters for 22 weeks and the carcinogen 9,10-demithyl-1,2-benzanthracene (DMBA) was the positive control (Figs 1 and 2). They found that, when applied separately, whitening products were not carcinogenic, that is, they did not initiate oral cancer when acting individually. In other words, hydrogen peroxide does not induce a normal cell to undergo mutations that progress into a malignant tumor. When a chemical substance induces such mutations, it is classified as an initiator. During the same trial, hydrogen peroxide was applied to the oral mucosa of other hamsters alternating with DMBA applications every other day during the same length of time. There was a considerable increase in the number of animals with oral cancer and in the size of the lesions, much greater than in the group of hamsters without DMBA. These results showed that hydrogen peroxide does not initiate, but stimulates the already induced cell proliferation and promotes the morphological appearance of cancer. Any chemical product that has such properties is called a promoter. Hydrogen peroxide is characterized as a promoter, but the term co-carcinogen has also been used. In the mouth, the oral mucosa and its cells are affected by several co-carcinogens: tobacco products, alcohol, sun rays, viruses and innumerable environmental chemical products, such as bicarbonate and herbicides and pesticides contained in foods. An oral promoter may very likely act and collaborate in the formation of a malignant tumor.

Using the same experimental model, Camargo[5] was mentored, as part of a PhD Program, to test once more the carcinogenic effect of 27% hydrogen peroxide and a specific whitening product containing 10% carbamide peroxide. At the same time, the effects of toothpastes with hydrogen peroxide in their composition were investigated.

FIGURE 1 - Normal lateral tongue margin and mouth floor in golden Syrian hamsters.

FIGURE 2 - DMBA-induced squamous cell carcinoma in lateral tongue margin and floor of the mouth of golden Syrian hamster after drug application on alternate days for 22 weeks.

First, 30 commercial brands of toothpaste were evaluated to detect hydrogen peroxide; 29 had it, although most did not inform about its presence on their labels. Toothpastes for children also had hydrogen peroxide.

The results found by Camargo[5] revealed that, in the composition of tooth whitening products or as part of toothpastes, hydrogen peroxide was a promoter of chemical oral carcinogenesis; that is, it was a co-carcinogen. These results confirm previous findings.

Figure 3 schematically shows the synergism that might exists between an initiator and a promoter. The promoter, which may be a whitening product, is graphically represented by drops, whereas the initiator, represented by the switch, may be tobacco products or alcoholic beverages. The schematic diagram suggests that tooth whitening in a smoker—for example, often performed by the dentist using a protective resin dam once a year—may represent the promoter that acts after the initiator, at alternate time points, which corresponds to the 6th situation (Fig 3).

Clinical, social and commercial implications of these results

The first implication of these recent findings is the need to inform the population about the benefits and risks of tooth whitening to promote a culture of open communication rather than a

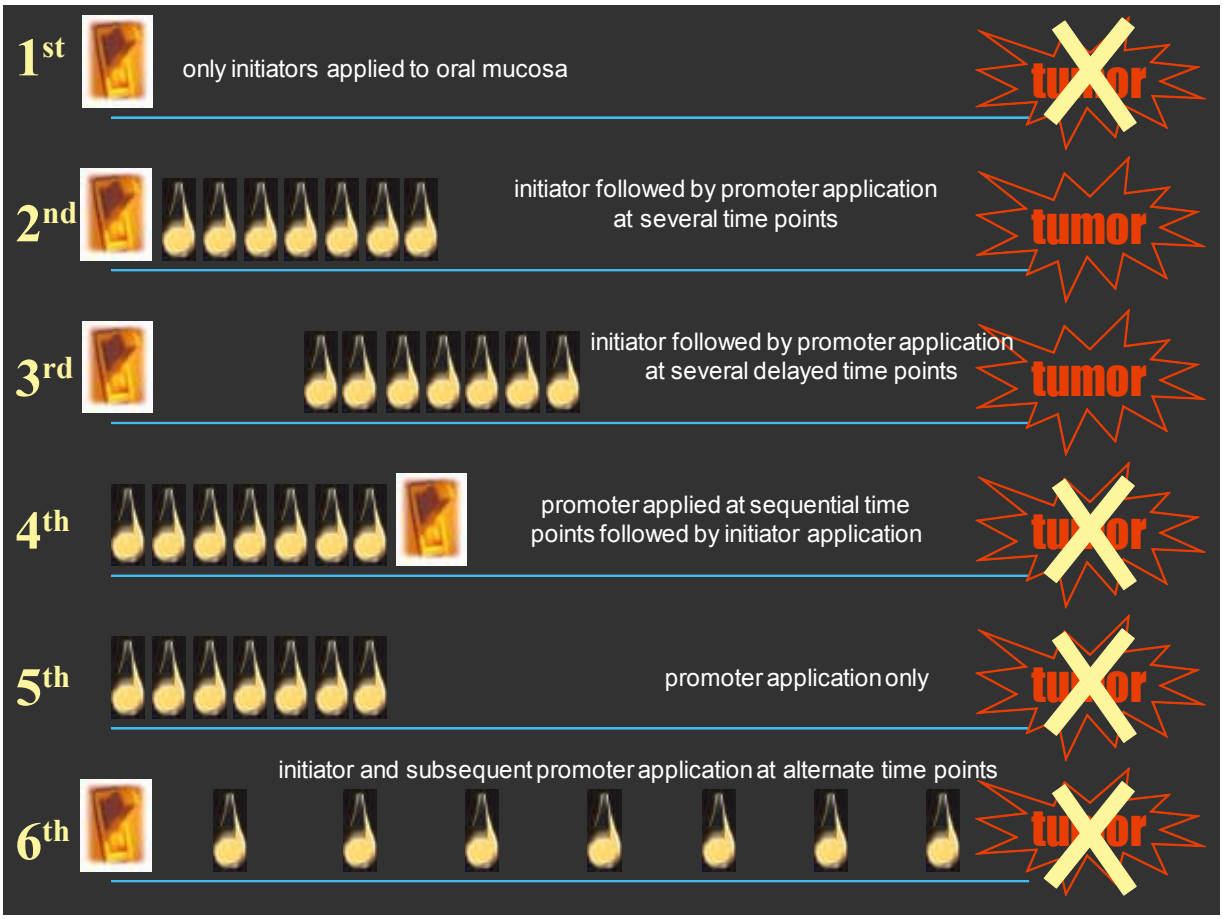

FIGURE 3 - Schematic drawing of six different situations of effectiveness of carcinogenesis promoting agents according to action time and frequency before or after use of initiating agent. According to tests using the experimental DMBA-induction model in oral mucosa, tooth whitening products act as chemical carcinogenesis promoters (switch represents initiator, and drop, promoter).

culture of fear. Undoubtedly, tooth whitening products are part of our current culture, but we should develop techniques and technologies to reduce and eliminate their undesirable effects. Tooth whitening is a personal opportunity, and the market should make it available to those that are interested in it. However, it should be safe, and the conscious choice of those that decide not to do it should be respected. Toothpastes and mouthwashes free of hydrogen peroxide should be offered to the population in general, and their composition should be described on their labels, as it is already the case with cigarettes, alcoholic beverages and oral antiseptic products.

The carcinogenic effects of hydrogen peroxide as a promoter are not limited to the oral mucosa, and extend to the oropharynx, esophagus and bowel[24-27] if ingested by the patient. Consumers should be warned not to ingest hydrogen peroxide during tooth brushing and oral hygiene, performed several times a day. Once again, consumers should be given the option to choose products with or without hydrogen peroxide.

People should be told that the carcinogenic effect of tooth whitening products is very mild, but its relevance is associated with the frequency at which hydrogen peroxide is in contact with the oral mucosa: every day, several times every 24 hours. They should also be warned about the fact that initiating factors, such as tobacco, alcohol, oncogenic viruses and products ingested with foods and breathed in the environment, are the most important causes of oral cancer. In carcinogenesis, whitening products are one of the several contributing factors, but are not capable of inducing cancer if used alone and exclusively, as schematically demonstrated in Figure 3.

Healthcare professionals, consumers, manufacturers and agencies should harmoniously get together to discuss what is best for society: to classify whitening agents as cosmetic products or as medical drugs. Cosmetic products, by definition, do not have a therapeutic action and cannot affect body physiology; however, tooth whitening products change dentin structures and have antiseptic effects. Should they not be, therefore, classified as medical drugs?

Another question should be raised: how about tooth whitening performed by the dentist in the dental office? Would it have the same carcinogenic effect? No, because tooth whitening performed by the dentist has undergone technical and technological improvements in the last 15 years. Tooth whitening applied in the office by the trained and prepared dentist includes the isolation of teeth, which may be achieved by using different techniques, such as cervical and gingival light-cured resin dams, which prevent the direct contact between the mucosa and the tooth whitening product (Fig 4).

At the same time, isolation of the gingiva and the cervical region protects the cemento-enamel junction and its dentin exposure gaps from the direct contact with the whitening products, whose action might enlarge the gaps and the diameter of exposed dentinal tubules and increase dentinal hypersensitivity.

After the conclusion of the whitening procedure in the dental office, and before water is used and the cervical and gingival resin dam is removed, maximal suction should be applied to remove the whitening product. After that, water jets can be used, but only when almost all whitening product has been removed using as much suction as possible, and after the resin dam has been removed, because some of the product, though not much, may remain in the dam's structure. This procedure will ensure that the amount of whitening products that is in direct contact with the oral mucosa and cemento-enamel junction is very little, particularly if we consider that this procedure is performed only a few times and not everyday, differently from tooth brushing and oral hygiene with mouthwashes.

Another question should be raised in this analysis of clinical and social implications of the can-

FIGURE 4 - Protective resin dam applied to cervical region; it drastically reduces or prevents contact of whitening product with gingival mucosa and cementoenamel junction.

cer promoting effects of tooth whitening products: Are the risks greater when tooth whitening is applied at home and prepared by the patient with or without professional supervision?

No matter how clear the information received from the dentist was, how well the nightguard fits the teeth, or how skillful the patient is, the whitening product will, unfortunately, spread on the oral mucosa, dissolve in the oral cavity and be carried away by saliva. The widespread and prolonged contact with the oral mucosa and the oropharynx will be inevitable. As product ingestion may also be unavoidable, the product will get in contact with other points of the gastrointestinal mucosa, which may have undesirable consequences. Whitening products have an extensive and unrestricted effect on the cemento-enamel junction.

In addition to these concerns resulting from the limitations of control when using at-home tooth whitening, two other important aspects should be mentioned:

1. The risks of self-medication or self-indication when the patient buys the product without first seeing a dentist or receiving any professional advice and applies it at home irregularly and not adopting any special care.
2. The lack of control over time and frequency at which the patient performs the procedure at home, which might enhance whitening results, but biologically affects the mucosa and teeth and does not compensate for the non-measureable and non-detectable risks in the future.

Final orthodontic considerations

External tooth whitening is a very important option to improve and enhance the appearance of teeth and the face after the conclusion of orthodontic treatment. Bracket bonding, accumulation of bacterial plaque, white spots and staining of lamellae, cracks and other cavities on the tooth surfaces may affect the esthetic results of the orthodontic treatment. External tooth whitening may standardize tooth color and remove stains from recesses. Together with restorations, drilling and other procedures, external tooth whitening may be a procedure to achieve part of the patient's final goal when undergoing orthodontic treatment: to give the mouth and teeth a normal and healthy appearance and, consequently, to improve personal relations and self-esteem.

Patients may ask for advice, and orthodontists may or may not indicate external tooth whitening. They should keep in mind that it is a technical procedure to be performed by a trained dentist aware of the possible biological effects of the chemical product used (hydrogen peroxide). This procedure should be restricted to the office, where carefully performed techniques and professional responsibility are part of the service paid by the patient. Tooth whitening performed at home will never have the technical accuracy and biological safety necessary and provided by the dentist: whitening products may spread over the teeth, cemento-enamel junctions and oral mucosa, and some of it will be swallowed.

Patients may also ask for recommendations about the use of toothpastes or mouthwashes. Products with tooth whitening agents, particularly toothpastes and mouthwashes, should bring that specific information on their packaging, where it

should read whether or not it contains hydrogen peroxide.

The effect of tooth whitening on teeth and oral mucosa are not measurable in time because of superposed factors that act in the oral cavity, particularly those that may cause oral cancer. Patients should receive information about the carcinogenic effect of whitening products, which is low. However, healthcare workers that prescribe them have much greater responsibilities and should also advise patients about preventive procedures and safety.

Health agencies, dentists, consumers and manufacturers, that is, society as a whole should harmoniously promote tooth whitening products to the category of medical drugs and restrict their use to dentists, who are duly trained and qualified to perform the highly technical tooth whitening procedures. Recommendations to use or purchase and requests to fill prescriptions should only be made by dentists.

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