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REVIEW

Undesirable and adverse effects of tooth-whitening products: a review

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Abstract Hydrogen peroxide (H_2O_2) is a powerful oxidising agent. It gives rise to agents known to be effective bleaching agents. The mechanisms of bleaching involve the degradation of the extracellular matrix and oxidation of chromophores located within enamel and dentin. However, H_2O_2 produces also local undesirable effects on tooth structures and oral mucosa. In clinical conditions, the daily low-level doses used to produce tooth whitening never generate general acute and sub-acute toxic effects. Genotoxicity and carcinogenicity only occur at concentrations that are never reached during dental treatments. Some transient adverse effects have been reported on the oral mucosa and the digestive tract if the product is swallowed. Local effects may occur on the oral mucosa and dental tissues during whitening, namely, pulp sensitivity, cervical resorption, release of selected components of dental restorative materials, and alteration of the enamel surface. Most of the local effects are dependent of the technique and concentration of the product so far used, but as the results of bleaching obtained are not stable, repeated treatments add to the adverse effects. The informed decision to administer or not and the control of bleaching effects should stand in the hand of dental surgeons and certainly not as it appears at present, as cosmetics sold without any restriction despite the potential health hazards of peroxides.

Keywords Tooth whitening · Hydrogen peroxide · Cytotoxic effects · Genotoxicity · Carcinogenicity · Resorptions · Hypersensitivity · Enamel surface

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Introductory remarks

Genetic diseases such as *dentinogenesis imperfecta*, or *dentine dysplasia* or some forms of *amelogenesis imperfecta*, some acquired foetal and post-natal pathologies occurring during tooth formation such as medical diseases (i.e., icterus, congenital erythropoietic porphyria, cholestasis, and renal diseases), treatments with tetracycline, or chronic ingestion of fluoride during childhood, may induce unacceptable levels of intrinsic tooth staining that should be included in the list of handicaps. In such cases, there is a real need for bleaching, mostly for psychological reasons and also for an improved social life of the patient [19, 22, 49]. Bleaching procedures are effective and certainly less destructive than any full or partial prosthetic restoration.

However, there is currently a wide range of bleaching techniques used for aesthetic reasons, and in many cases, such treatments are not necessary. As a consequence, the wide diffusion of whitening methods have to be controlled because it is well known that there is no therapy without high or small risks. When these methods are used correctly, there are only minor consequences and, therefore, a clinical tolerability. In contrast, abuses approach the limits of risks and this should be taken into

consideration or better documented prior to taking a clinical decision.

Tooth-whitening treatments are carried out either at the chair-side by dental surgeons ('in-office') or by 'staff-supervised in-office bleaching', or as 'at-home' dentist-supervised treatments, or bleaching devices are sold over-the-counter (OTC) to patients and may be used without any control of dental practitioners [11, 19]. Each method is effective for most staining but needs different periods of time to obtain the expected result. When strips are used as typical OTC treatments, 31.85 cycles of 15 min are necessary to obtain some whitening; whereas, at-home dentist-supervised bleaching needs 7.15 cycles and in-office treatment needs 3.15 cycles [11].

In many countries, no final decision has yet been taken by state agencies for sanitary security to classify the bleaching agents as medical devices or cosmetic products, or both, depending on the final concentration of the gel. Whatever the decision will be in this matter, up to now, the active compounds are, in general, the same although the doses administered can differ substantially. Between 1918 [1] and the 1990s [66], sporadically, a few publications reported that bleaching could be obtained clinically, but most studies were published in the last 20 years [9, 69]. Bleaching effects are mostly based on the effects of carbamide peroxide, releasing about 33% of their content as hydrogen peroxide (H_2O_2). H_2O_2 can act as a powerful oxidising agent and can give rise to agents known to be effective bleaching agents (i.e., its corresponding mono-anion (HO_2^-) and hydroxyl radical (OH)). In addition, carbamide peroxide also releases urea, which is rapidly decomposed into carbon dioxide and ammonia [22, 41]. Chemical reaction of the two reagents with the organic extracellular matrix components (ECM), including pigments or chromophores, constitutes the chemical basis of tooth whitening.

It is well documented that urea degrades the organic matrix located in the enamel [8, 31, 32]. The organic matrix constitutes 0.6% in weight and 4% in volume of the total human adult enamel. Urea and ammonium ions $(NH_4)^+$ act on the hydrogen bounds that are crucial regarding the secondary, tertiary, and quaternary structures of matrix proteins. After the initial alteration, the degraded proteins are further split into small peptides, released, and finally eliminated from the mature enamel [8, 31, 32, 41, 57]. The same applies to most non-collagenous dentin matrix components. The empty minute spaces that are rendered accessible by urea allow the diffusion of hydrogen peroxide throughout the whole thickness of enamel up to the dentino-enamel junction (DEJ).

Bleaching agents cross the DEJ and interact in the subjacent dentin with the chromophores, pigments, and ions that are now recognised to be responsible for tooth staining. The removal of ECM is not homogeneous. In enamel, it is mostly detectable in some rods and not apparently associated with inter-rods [31, 32]. The removal of matrix components is associated with the loss of some hydroxyapatite crystals, bound at specific areas where there is a local accumulation of matrix components. Consequently, minute craters form at the enamel surface as a reaction to an efficient peroxide treatment [24, 60, 62, 93]. The balance between the need for treatment that is judged necessary by the practitioner and the risk induced by the therapy has to reach a valuable equilibrium. It is clear that many efforts of the industry were carried out in order to minimise the noxious effects of bleaching products. However, there is clearly a compromise between efficiency and safety that cannot be ignored [11, 19].

Adverse effects of bleaching agents have been reported after the treatment of non-vital teeth [69]. When applied to vital teeth, tooth sensitivities, the alteration of enamel surfaces, and the consequences arising from the release of some components of restorative materials have been reported [22] and are important phenomena to consider. The effects on the oral mucosa are controversial and depend on the technique that has been employed. It is also the case that the effects of bleaching agents on the digestive tracts of both animals and humans have to be considered in detail. The conclusions of in vitro and animal studies should be adapted to the human situation. Finally, general toxicity, genotoxicity, and carcinogenicity are also important considerations that have to be taken into account in the frame of safety or tolerability [57, 82, 85].

A review of the potential effects of bleaching agents is not facile, largely because of the many divergent reports that have been published on a range of important aspects of this area. There are multiple reasons for these conflicting reports. In some cases, what has been published arises more from the marketing and advertisement of products rather than that from unbiased scientific investigations, and it is not always a simple process to decide what has to be kept on the list of reputable references. In many cases, however, diverging published data are mostly attributable to differences between the concentrations of the bleaching reagent that was used, the reagent itself, and even the carrier, which may also play an important role in the reaction (or lack of it). In any case, taking into account the many excellent reports that are available, it is necessary to consider the limit above which there is a risk of undesirable side effects. An excellent review article has been published in 2003, and we have to acknowledge that it constitutes one of the major references in the field [22]. However, since the last 6–7 years, new experimental results were obtained and new products were put on the market. These additional data are incorporated in this review.

General and local toxic effects of hydrogen peroxide

Allergic sensitivity

No allergic sensitivity has yet been reported for carbamide or hydrogen peroxides, or for alternative peroxo-adducts, in contrast to the acute and sub-acute effects that are well documented.

Acute cytotoxic effects

Acute cytotoxic effects appear at doses over 5 g/kg/day for a product containing 10% (*w*/*w*) carbamide peroxide [44, 88]. This corresponds to a 0.3 to 1.8 mg/kg (body weight)/day H_2O_2. Force-feeding rats directly into the stomach with 5, 15, and 50 mg of carbamide peroxide/kilogramme, or its equivalent in tooth-whitening products, induce dose-dependent ulcerations of the mucosa, easily detectable 1 h after feedings; however, these heal after 24 h. This reaction is not observed for doses lower than 15 mg/kg. The gel associated with peroxides in a commercially available product seems to enhance the toxic effects. No adverse effect has been detected in the kidney or liver [21].

From these data, assuming a threshold of toxicity of 15 mg of carbamide peroxide/kilogramme and a security factor of 100, it is apparent that at a carbamide peroxide concentration of 10 mg (equivalent to 3.6% (*w*/*v*) H_2O_2), we are at the limit of systemic effects for a 70-kg man [21]. In this context, it has been reported that a 16-month-old child died after ingestion of a 3% (*w*/*v*) H_2O_2 solution. However, this accident was at the lowest doses so far reported. From the available data, we can conclude that the everyday doses used during whitening procedures is close to a level where adverse systemic effects might occur.

Sub-acute toxic effects

There are no effects or, at least, no reported effects in humans. In animals, the daily critical doses should be lower than 30 mg/kg/day for the rat and 26 mg/kg/day for the mouse.

After topical application to humans, °OH radical derived from electron transfer to H_2O_2 can, in principle, induce lipid peroxidation, and also DNA alteration followed by cell lysis and death [41, 57]. Anti-oxidants and iron chelators may prevent such reactions, the former by scavenging °OH or lipid peroxyl radicals (LOO°), the latter by complexing Fe(II) and attenuating its ability to participate in Fenton-type reactions. The enzyme catalase inhibits these reactions via its capacity to directly consume H_2O_2; whereas, the lipid-soluble antioxidant vitamin E (α-tocopherol) blocks such damage by scavenging LOO° radicals [57, 82].

H_2O_2 induces squamous metaplasia on tracheal explants at concentrations of 50–100 μmol/l; whereas, cytotoxic effects appear at a concentration ≥500 μmol/l [71]. At 700 μmol/l, H_2O_2 induces embryonic fibroblast necrosis; whereas, at 150 μmol/l, apoptotic effects are induced [34]. In another report, it is shown that when 35% (*w*/*v*) carbamide peroxide is used, the percentage of viable cells is decreased to 60% in comparison with control cells (FM3A cell line). This value falls down to 43% with a 20% (*w*/*w*) carbamide peroxide gel. The level of toxicity is 50 and 40 μg/ml, respectively. An extrapolation to a 70-kg individual suggests that in order to remain below the risk doses and avoid any toxic effects, the daily dose used should be ≤10 mg carbamide peroxide, or its 3.3 mg H_2O_2 equivalent [7].

Genotoxicity and carcinogenicity

International Agency on Research on Cancer data [44] do not refer to any mutation or cancer risk attributable to professional exposure. However, in animal models, adenoma and duodenum carcinoma have been detected experimentally after oral administration of H_2O_2. In the mouse, hyperplasia appears in the gastric mucosa in 20–42% and duodenum hyperplasia in 40–62% of the experimental animals 8 weeks subsequent to the ingestion of 0.10% or 0.40% (*w*/*v*) H_2O_2 solutions. These reactions are more substantial in the duodenum than the stomach. In addition to gastric mucosal ulcerations after force-feeding with 15 mg/kg carbamide peroxide, adenoma and carcinoma were observed. This pathological transformation seems to be strain-dependent and linked specifically to the catalase activity of the different groups of mice [45–47]. Critical analysis of the experimental situation leads to conclude that hydrogen peroxide is not a carcinogenic thread, at least for the digestive tract [23].

It seems unlikely that H_2O_2 may induce cutaneous cancers [13, 52]. In the oral cavity, repeated applications of 30% (*w*/*w*) H_2O_2 produce hyperkeratosis, hyperplasia, and dysplasia with weak intensity after 22 weeks [71, 89] However, no tumours were detectable with H_2O_2 alone. This is not the case when a carcinogenetic agent is co-administered with H_2O_2 [89]. However, it is documented that H_2O_2 inhibits gap junctional intercellular communication in glutathione-sufficient but not in glutathione-deficient cells, and an aberrant intercellular junctional communication has been implicated in tumour promotion, neuropathy, and teratogenesis. This sheds light on potential dangers and on some genetic aspects of the reaction [87].

H_2O_2 has been shown to be mutagenic in a number of strains including *Salmonella typhimurium* and *Escherichia coli* [2]. In some cell cultures, H_2O_2 treatment induces DNA strand breakage and is mutagenic, especially toward cells from the L5178Y murine lymphoma subline. For

example, at 37°C, LY-R are 3.6 times more sensitive to the killing effects than LY-S cells; whereas, at 4°C, they were 11 times more sensitive [53]. Mutagenicity has also been reported in V79 Chinese hamster cells, and the reaction is concentration dependent. Ziegler-Skylakakis and Andrae [94] concluded from their investigations that at a solution level of 4 mM H_2O_2, the mutation frequency increased sixfold above the controls, and the extent of survival was reduced by 50%. DNA fragmentation has also been observed in human lymphocyte cultures and epithelial cells of the respiratory tract.

Following the use of hydrogen peroxide at a concentration of (10 μmol/L), Timblin et al. [84] observed the overexpression of the proto-oncogen *c-jun*, a process which leads to cell proliferation.

It should be added that despite all the potential risks inherent with the use of peroxides, up to now there is no report of human cases where carcinogenic effects are actually established [23, 57]. However, two recent publications pointed out that hydrogen peroxide used in long-term treatment and at a high concentration might act as a promoter of oral mucosal damage and, moreover, have genotoxic and carcinogenic effects [65, 85].

Local effects of bleaching agents on dental tissues and oral mucosa

The whitening effects of hydrogen peroxide on teeth and oral mucosa are well documented [11, 18, 49, 55, 67]. However, in a limited number of cases, undesirable effects such as hypersensitivity (2.62–3.38%) and gingival irritation (0.23–0.85%) have been reported [11, 54]. Changes in enamel microhardness, micromorphological defects due to demineralization, and effects on restorative materials have also been reported [17, 24, 43, 60, 62, 64, 68, 77, 80, 81, 90–93].

Effects on non-vital teeth (internal and/or external treatment): internal and external resorptions

Some time after a root canal treatment, the colour of the treated tooth changes and gradually becomes unaesthetic [74]. This is very often the case for incisors after a local trauma. Darker or brown-grey teeth may be subjected to a whitening treatment that removes less dental tissue than the preparation of a jacket crown or a veneer. In most studies, however, no adverse reaction has been observed after such treatments. Indeed, no resorption was detected in a series of 100 and 250 patients, respectively, that have been treated and recalled for a follow-up [6, 42]. However, external resorptions have also been reported in a further series of patients. About 7% of the teeth displayed resorptions in 58 cases, monitored during an 8-year period [26]. The frequency of resorption is certainly dependent on the bleaching method that has been utilised. A mixture of sodium perborate and 3% hydrogen peroxide was shown to induce delayed outer resorptions, which appeared 12 years after the treatment. Heating the bleaching solution enhances the number of resorptions that are induced [69].

Exactly why such external resorptions are occurring is poorly understood. They seem to be dependent on the pH, the trauma, and the heating procedure that was used. They appear a few years after the bleaching treatment, and we are still unable to control them. The origin of the pathology could be an enhancement of bacterial penetration inside dentine tubules [40]. This invading pathway may be also related to some structural defects or pathological alterations of the cementum that favour such bacterial penetration [74]. Apparently, no correlation was found between the mechanism of action of sodium perborate and the adhesive properties of macrophages. It seems that these cells do not play a role in the resorption process [48]. Tissue permeability in the cervical area of the tooth may be implicated in the initiation of such resorptions. However, there is no predictable evidence from clinical examination that such lesions will form. Therefore, before taking the decision to administer a whitening treatment on non-vital teeth, it is important to consider that resorption may be induced. The final outcome of such cervical resorption is the fracture of the crown, when the lesion reaches a certain volume. This, unfortunately, leads to a residual root that cannot be employed for a prosthetic device and, hence, has to be extracted.

Effects of external treatments on vital teeth

Post-treatment hypersensitivity and pulp alteration

When a 10% (*w*/*w*) carbamide peroxide treatment is conducted, between 15% and 65% of the patients receiving it display sensitivities of the treated teeth within the next 4 days [38, 54, 78], far less for other authors (2.62–3.38%) depending on the bleaching product and the concentration used [11]. The sensitivity is higher with H_2O_2 combined with the thermo-catalytic enhancement at some point following the chair-side treatments [69]. This sensitivity may last up to 39 days and, in some cases, is so painful that it leads to treatment interruption. It is well documented that H_2O_2 diffuses throughout the enamel layer and dentine, even in vital teeth. In vitro studies demonstrate peroxide penetration into the pulp with most bleaching agents and methods, including whitening strips that presumably would excerpt mild effects [28–30]. This phenomenon results from both the osmotic and vascular pressures [35]. The physiopathological

mechanisms of sensitivity or pain are however not fully understood. Nerve endings are undetectable in enamel. Contemporarily, it is well documented that nerve endings are present in the inner dentin in an area near the periphery of the pulp (150 μm thick), visualised either by radioautography [15] or by immunocytochemistry [58]. The absence of nerve endings in the outer dentine and at the DEJ clearly does not assist us in interpreting the phenomenon. The hydrodynamic hypothesis developed by Brännström [14] may apply here, i.e., backward and forward movement of the "dentinal lymph" may be transmitted to odontoblast processes located inside tubules and then to cell bodies where a direct anatomical link occurs between odontoblasts and nerve endings in what is known as the sub-odontoblastic plexus. Bleaching agents containing H_2O_2 in high concentration may favour bacterial penetration through dentinal tubules [40]. In view of the mild irritative process, reactionary dentine is formed which gradually reduces the hypersensitivity. Alternatively, there is peritubular dentine formation after such stimulation, resulting in an eventual reduction of diameter of the lumen of the tubules. The two processes may be interdependent.

Diverging results have been published with respect to the consequences of the influence of whitening treatments on pulp. According to Seale et al. [79], a 35% (*w*/*v*) hydrogen peroxide gel used for 30 min induces severe pulp reactions in dog teeth. The odontoblast layer is reduced and even disappears in the area facing the treated part of the tooth. The predentine is missing. Inflammatory cells are present at the pulp surface, and internal resorbing processes may be observed 4 days after the treatment. The inflammatory reaction is present for a period of 15 days, together with the dilation of blood vessels, vascular thrombus, and haemorrhages. Fortunately, these alterations disappear after 2 months. Another report reveals translocation of odontoblast nuclei in dentinal tubules in 32% to 53% of treated human teeth, without any pulp reaction [20]. The differences between these two reports do not appear to be ascribable to compositional differences between the two bleaching agents which were used, since they both contained 35% (*w*/*w*) H_2O_2 coupled with thermal enhancement. A more recent study provides evidence for a moderate reaction with 10% (*w*/*w*) carbamide peroxide [5]. Moreover, it should be noted that bleaching methods induce an increase of endogenous pulp peroxide (mean value, 0.44 mM). However, this was 3,000 less than that which can induce acute pulp damages arising from enzyme release [50]. In any case, tooth sensitivity resumes gradually, without any long-term adverse effects.

Sensitivity can be prevented or decreased by treating the teeth 30 min prior to whitening by desensitising agents containing 3% potassium nitrate and 0.11% per weight fluoride [56].

Alteration of enamel surface: consequences on bacterial plaque adhesion and cariogenicity

In this area, reports on the effects of whitening gels are also divergent. Some researchers have reported either no effect on or only minor changes to the enamel surface or the subsurface [18, 37, 50, 51, 64, 90–92]. In contrast, others have shown moderate to severe enamel surface modifications [24, 27, 60, 62, 80, 93]. Again, it is difficult to have a clear-cut idea on the actual situation. The divergent results that were obtained are mainly attributable to differences in the protocols, the chemicals that were used and their concentrations, and also may be influenced by the method used to visualise the effects. In some case, the reliability of the results is related also to the scientific independency of the researcher and is also apparently linked to the scientific quality of the journal where the report is published.

Although some authors have pointed out that tooth bleaching with selected commercial H_2O_2 or carbamide peroxide do not produce modifications in surface morphology [81–83], another group of reports found that bleaching agents create some enamel porosity [21, 54, 56, 84]. For example, Ruse et al. [77] have shown that in bleached enamel, the calcium/phosphate ratio is altered by a 35% H_2O_2 treatment. According to Seghi and Denry [80], enamel treated with a 10% (*w*/*w*) carbamide peroxide gel displays a reduction in apparent fracture toughness (ca. 30%), with no significant changes in surface hardness. Data acquired indicate small but significant decreases in abrasion resistance. To explain these findings, the authors hypothesised that the chemical action of H_2O_2 induced an alteration of the organic matrix of enamel. Differences between these published reports may arise from a variation in the concentration of chemical bleaching agents, e.g., a concentration of 35% (*w*/*w*) carbamide peroxide (11–12% H_2O_2) affects the structure of enamel; whereas, 10% or 16% (*w*/*w*) have no effect [68]. From the published literature, it could be concluded that bleaching treatments induce changes in surface roughness and consequently influence the formation of supra- and sub-gingival plaque [70]. Therefore, the adhesion of *Streptococcus mutans* to enamel is increased [43]. This is also the case for *Streptococcus sobrinus*, but not for *Actinomyces viscosus* [63]. Such undesirable effect may have some implication on future developments regarding the carious decay. However, to the best of our knowledge, it should be recognised that up to now, there are no clinical report available on the potential development of caries from a broad series of whitening treatments. However, it may be assumed that with the development of such methods, we may face such consequences in the near future.

An investigation performed with the atomic force microscope revealed that commercial bleaching agents as

well as a 30% (*w*/*v*) H_2O_2 solution enhanced groves present at the surface of enamel and also act on its inner structure [39]. Hence, it may be concluded that most bleaching agents (even those containing 10% (*w*/*v*) carbamide peroxide), induce slight to moderate alterations of the enamel surface and a decreased enamel microhardness, variations between the bleaching agents employed were clearly notable [73]. These microlesions are of much lesser importance than those arising from etching with phosphoric acid. From some reports, it appears that minor defects are also induced in the subsurface. These defects might interfere with the adhesive properties of restorative materials. After some time, the porosities are gradually reduced. In view of enamel abrasion, and also as a result of ion re-precipitation controlled by some salivary proteins and/or by the bacterial plaque, calcium-phosphate precipitation occurs inside the porous enamel, a phenomenon that leads eventually to re-hardening and furthermore contributes to a return to the normal situation.

Therefore, the concept that "in-office" bleaching is a non-destructive cosmetic procedure should be reconsidered, and this apply also to the other whitening procedures. It should be considered that enamel demineralization is an undesirable effect resulting from bleaching agents, related to their concentration and to the time necessary to obtain teeth whitening. Along this line, strips may have less destructive effects, although peroxide release in saliva is higher by using some strips in comparison with trays charged with gels [36]. Remineralization due to saliva may restore gradually the mineral charge of enamel surfaces, but the specific organic matrix is definitively degraded, and this alteration may interfere with enamel repair. Attempts to reduce the loss of mineral and the formation of micro-defects on enamel surface were carried out with fluoride-containing bleaching agents shown to induce less enamel surface demineralization and altered microhardness [17].

Effects of tooth-whitening peroxides on the oral and gastric mucosa

When the dental surgeon at the chair-side applies H_2O_2 or alternative peroxo-adducts, there is a clinical control of the risk factor for developing gingival irritation. This is not always the case with nightguard, i.e., dentist-prescribed home-applied bleaching methods. The situation may be even worse when patients without any control of a dental surgeon are using whitening methods. Carefully adapted trays are mandatory if the dental practitioner wishes to prevent or suppress gingival irritations.

H_2O_2, together with lauroyl and benzoyl peroxides, all represent compounds with the potential to generate free radical species. They are not carcinogenic when applied topically to the mouse skin, but they are potent skin irritants. Notable modifications induced by peroxides in skin are epidermal hyperplasia and the induction of dark keratinocytes: 15% or 30% (*w*/*v*) H_2O_2 gave rise to an extensive epidermolysis, inflammation, and vascular injury in rodents. This was found to be followed by a rapid regeneration and epidermal hyperplasia [52]. After topical application of 10% (*w*/*v*) carbamide peroxide, an increase in the quantity of cells located in the basal layer of the oral mucosa revealed by proliferating cell nuclear antigen (PCNA) staining was noted [3]. However, by immunodetection of cyclin D and p16 (representing a proliferation marker and a negative regulator of cell proliferation, respectively, the alteration of which are considered as markers of an initial cancer formation), studies carried out on the oral mucosa failed to indicate any significant alteration [33]. In contrast, using the PCNA as a marker, the same researchers have shown a transient proliferation after topical application of carbamide peroxide to the basal and suprabasal epithelial oral border [3]. Therefore, the controversy is not yet solved.

In fact, temporary burnings of the tissue arising from H_2O_2 have been reported. In the hamster pouch, severe inflammatory processes are now well identified. During the treatment of periodontal diseases, the bacteriostatic properties of H_2O_2 have been widely used, and in this context, cell lysis has been reported at a concentration as low as 1% [61].

Carefully adapted plastic trays or nightguards may reduce the amount of whitening agent that is expelled onto the oral mucosa when the patient overfills the tray. Strips and painted lacquers reduce the risk. The ingestion of bleaching gel may produce gastric pain, although the repeated ingestion of peroxide-containing gels does not seem to have severe consequences.

Effects on restorative materials: the release of mercury and silver from amalgams and adverse effects on the adhesive properties and on the margin of composites fillings

Bleaching agents have well-established effects on dental fillings [4, 10]. After treatment of silver amalgam with a gel containing 10% (*w*/*w*) carbamide peroxide, an increased level of mercury and silver was found near the surface of silver amalgam; whereas, tin and copper levels therein were diminished [75, 76]. In vitro, carbamide peroxide favours the release of mercury from silver amalgams. However, in vivo, the reaction is limited by the dental biofilm [83]. Mercury can be released up to 80 h after whitening treatment [72].

Such effects have been reported exclusively for silver amalgam fillings. These effects are not clinically detectable but have been reported from in vitro studies for other materials used in restorative dentistry. There are nowadays

convincing evidences that bleaching agents may influence bacterial adhesion, modify the surface roughness of polyacid-modified resin-based composites and resin-modified glass ionomer cements (see for review [10]). The interfacial fracture toughness of dentin/resin composite adhesive is affected, with significant reductions observed at 16% and 21% (*w*/*w*) carbamide peroxide concentrations, after 42 h [25]. The marginal leakage of resin composite restorations is increased after bleaching with 10% (*w*/*w*) carbamide peroxide, but not amalgam restorations [86]. Penetration of the pulp chamber by bleaching agents is common with resin-modified glass ionomer cement fillings; whereas, the lowest pulpal peroxide penetration is detected with the resin composite materials [28]. A 6% (*w*/*w*) H_2O_2 does not cause significant surface dissolution of glass ionomer, but the authors did not investigate the dentin-glass ionomer cement (GIC) interface [59].

Altogether, these data suggest that whitening treatments may induce alterations of the restorative material itself, impairs the conversion of dental adhesives after dentin whitening, or modify the interface between the biomaterial and dentine to the detriment of adhesive properties [10, 16]. Moreover, if the restorative material is present in the bleached surfaces, a significant reduction in the resin composite shear bond strength can be observed [12, 81].

The long-term effects of such methods are questionable in terms of public health costs, especially when they are used without the control of a dental surgeon.

Stability of tooth-whitening treatments and acquired exogenous staining

It is now well established that bleaching methods are efficient. After a few days or appointments at the chair-side, teeth lost one or two colour divisions on a tooth shade device, and patients are generally satisfied from the gain that is obtained. However, after some time, the initial staining colour returns, or in view of dental enamel permeability, a renewed level of exogenous staining agents penetrates and diffuses throughout enamel and even reaches dentine [19]. This is the case for tobacco smoke, tea, coffee, jams, and many other potential staining agents. As long as dental surgeons control the process, it is not an acute problem. However, when identified by the patient, the staining instability may lead to uncontrolled multiple treatments and, hence, the repeated re-exposure of enamel and gingiva to peroxo derivatives. It is also clear that the patient's conception of white teeth is mentally mediated and related more to social and sexual concepts rather than to a reality, but the end-point will be that some individuals will unnecessarily over-use whitening devices. As a consequence, demineralisations and local severe structural alterations may occur as a long-term effect of repeated bleaching, and sub-toxic or toxic doses may be inadvertently attained. The percentage of such patients is not known at present. Another open question is that on treatment with 10% to 15% (*w*/*w*) carbamide peroxide, efficient whitening results are easily and rapidly obtained. To be equivalent to a process involving 10–15% (*w*/*w*) carbamide peroxide for 2 weeks, a treatment conducted with a lower concentration such as 5% (*w*/*w*) should be performable for ca. 3 weeks. Although in the latter treatment the dose of peroxide is lowered, the time required to reach a whitening effect is of course extended. Consequently, lower doses will involve longer treatments, although it could be argued that noxious effects may be similar [11, 55].

Finally, in order to match the colour of previously placed restorative material with the shade obtained after bleaching on natural teeth, fillings have to be replaced. Because tooth whitening is not stable, the colour of the fillings differs gradually from the frontal teeth and they need again to be renewed [19]. We reach here the limits of what can be acceptable between a dentistry primarily oriented on cosmetology and the biomedical clinical practise.

Conclusions

Despite the rather contradictory conclusions arising from an analysis of the literature, it appears that the chemical mechanisms of bleaching agent actions involve alteration or destruction of the enamel organic matrix, a phenomenon that allows the diffusion of peroxides throughout enamel toward dentin where the chromophores are oxidatively decolourised. From an analysis of the available data, we can conclude that

1. Bleaching causes small defects at the surface and subsurface of enamel.
2. Dentin permeability is probably modified and, as a consequence, post-treatment transient tooth sensitivity is observed in many cases.
3. The effects on pulp are more controversial and may be inconsistent. Nevertheless, chronic treatment with peroxides may be not safe, and this could be the case when such treatments are carried out in the absence of a sufficient level of control by dental surgeons.
4. Effects observed regarding dental restorations are well recognised, there is a release of mercury from amalgam fillings, and bleaching methods alter the interface between dental tissues and glass ionomer cements or resin composites.
5. The bleaching of non-vital teeth may induce resorption in the cervical area in an unpredictable manner.

6. The long-term effect of bleaching on the development of carious decay has not yet been demonstrated but cannot be ignored.
7. Gingival lesions appear in relation to the uncontrolled applications of whitening gels. Again, the cellular and tissular mechanisms of peroxide damage are well elucidated, and again there is a critical requirement for qualified control in order to avoid long-term gingival tissue damage.
8. The ingestion of peroxide may occur when poorly adapted trays are employed.
9. At the doses that are administered, it is clear that up until now, there is no indication of any effects in terms of general toxicity, genotoxicity, and carcinogenicity in human. Therefore, there is a clinical tolerability. It is also clear that below a 3.6% (*w*/*w*) H_2O_2 concentration (10% (*w*/*w*) carbamide peroxide), there is apparently no toxic or sub-toxic risk.
10. Taking into account the possibility that chronic treatments might be applied as cosmetic products that are sold OTC, the higher concentrations utilised should perhaps be revised.

Altogether, all these local effects have to be taken into consideration prior to deciding if a whitening treatment is necessary or, for that matter, safe. Potential patients should be warned. There is a balance between the effects that may or may not appear and the real need for bleaching. In many cases, it seems rather an artificial cosmetic fashion requirement than a deserving cause. Finally, the informed and appropriate decision to administer or not, and the control of bleaching effects should stand in the hand of dental surgeons (or at least be under their control), and certainly not as it appears at present, as cosmetics sold without any restriction despite the potential health hazards of peroxides.

Conflicts of interest We have no conflict of interest.

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