

## Review Article

# Sensitivity in Dental Bleaching and the Use of Anti-Inflammatory Agents

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## Abstract

This study discusses the role of anti-inflammatory medications in reducing the sensitivity caused by tooth bleaching. Hydrogen peroxide ( $H_2O_2$ ), the active principle in bleaching agents, reacts with dental enamel on contact and produces oxygen, in the form of free radicals, and water. Because of the low molecular weight of free radicals, as well as the porous nature and selective permeability of enamel, the free radicals pass into dentin and through the dentinal tubules, to the pulp. In response to these stimuli, defense cells in the pulp tissue promote the release of inflammatory mediators, resulting in short-term tooth sensitivity that may be experienced as acute pain. Anti-inflammatory medications will reduce the inflammatory response, as these drugs act on the production pathways of the mediators. Drugs such as ibuprofen and etoricoxib should be thus effective in reducing tooth sensitivity. Among the medications used, however, only ibuprofen seems to reduce tooth sensitivity from bleaching.

## INTRODUCTION

Today's standards of beauty demand a good smile. Patients report that the teeth are the most important aspect of an attractive face [1]. As a result, dentistry offers multiple cosmetic procedures, with bleaching being one of the most popular services [2,3]. However, although clinically successful in most cases, tooth whitening has the disadvantage of causing dentin hypersensitivity, which is the main cause of discomfort and interruption of treatment [4,5]. Anti-inflammatory use before bleaching has been reported to reduce dental sensitivity during the whitening procedure [6], thereby increasing the patient's comfort and tolerance of bleaching treatment. This study discusses the role of anti-inflammatory medications in reducing dentin hypersensitivity caused by tooth whitening.

## Aspects of tooth bleaching

Tooth bleaching is one of the most conservative dental treatments to improve the smile's appearance, which is one reason why it has become so popular [2,7,8]. As their active principle, most currently used bleaching agents employ hydrogen peroxide ( $H_2O_2$ ), either directly obtained or as the product of a chemical reaction with carbamide peroxide or sodium perborate [9,10].

The whitening action of hydrogen peroxide is performed by its decomposition products, which include free radicals,

reactive oxygen molecules, and peroxide anions [11,12]. These highly unstable molecules can bind with organic or inorganic molecules, including chromophores (long-chain, complex, and heavy molecules that have a dark pigmentation) [9]. Free radicals bind to and break chromophores through oxyreduction, changing their optical structure and reducing their absorption of light. The chromophores are transformed into smaller, lighter-colored, and lower-molecular-weight molecules that can diffuse through the dentinal tubules and the enamel micropores [11,13].

In recent decades, much research has been undertaken to increase the efficiency and practicality of whitening treatment, encouraging changes and improvements. Today, patients can choose to have bleaching performed in the dental office or at home. The two treatments may even be combined, as studies for more than 10 years have affirmed [14]. In-office tooth whitening generally uses high concentrations of hydrogen peroxide (30–40%), presented as a liquid or gel. For this procedure, protecting the oral tissues is very important [15]. For home whitening, the concentrations are much lower (hydrogen or carbamide peroxides at 3–22%) [16]. Prescription whitening products (typically strips) have also lower concentrations of bleaching agents (5–10%) [9].

Despite its excellent cosmetic results, a common side effect of tooth whitening is dentin hypersensitivity, a symptom associated with resistance to the procedure on the part of the patient

[4,5]. In reports by Schulte et al. (1994) [17], 4 out of 28 people discontinued use of a home whitening treatment because of dentin hypersensitivity. The presence of dentin hypersensitivity is closely linked to the concentration of the bleaching agent and the length of application [18].

Although the literature has clearly established that dentin hypersensitivity is a side effect of whitening, what leads to dentin hypersensitivity during and after bleaching is not entirely clear. According to Markowitz [19], hypersensitivity during bleaching is related to the hydrodynamic theory. Free radicals from hydrogen peroxide diffuse through the enamel and dentin, promoting the movement of fluid present in the dentinal tubules, stimulating nerves, and generating sensitivity. In the same way, these free radicals reach as far as the dental pulp, inciting an inflammatory response of the pulp cells and unleashing perioperative hypersensitivity [20-23].

To reduce the uncomfortable side effect caused by inflammation of the pulp during bleaching, researchers have investigated the use of anti-inflammatory medications. These drugs act on the production pathways of the mediators of inflammation, blocking them and reducing hypersensitivity [24].

### Dentin hypersensitivity

Dentin hypersensitivity can be defined as an acute, short-term pain in response to heat, tactile, electric, osmotic, chemical, or evaporative stimuli that are not caused by any other pathological condition [25]. Dental hypersensitivity is an increasingly common condition that limits patients' day-to-day habits, such as having hot and cold foods and drinks. In Brazil, research performed by Fischer et al. (1992) [26] showed that 25% of those who participated in the study reported the presence of dentin hypersensitivity, with 17% of those cases confirmed by clinical exam.

The etiology of dental hypersensitivity is related to factors leading to the exposure of the dentinal tubules to the oral cavity. Examples include abrasion, erosion, attrition, gingival recession, scraping and coronal-root smoothing, and tooth whitening [27]. Sulieman (2008) [28] reported that dentin hypersensitivity occurred in two-thirds of patients during bleaching [28]. Other factors, such as age, sex, oral pH, and inadequate occlusion, can affect dentin sensitivity [29].

The dental structure normally identifies and responds to external stimuli because dentin has structural and function relationships with the pulp [30]. The dentinal tubules play an important role in transferring stimuli (including harmful stimuli) to the pulp [31]. By contrast, the presence of dentin hypersensitivity is related to the exposure and opening of the dentinal tubules [25,32]. In intact dentin and dentin without sensitivity, nearly all of the dentinal tubules are occluded [33,34].

Various theories have been developed to explain the mechanism behind the pain caused by dental hypersensitivity. These theories include the odontoblastic transduction theory, the neural theory, and the hydrodynamic theory, with the last being the most accepted one. Brannstrom (1963) [36] proposed the hydrodynamic theory. It postulates that thermal, physical, or osmotic stimuli change the fluid present in the dentinal tubules, unleashing hydraulic modifications, promoting fluid movement,

and leading to rapid outward flow and pressure changes through the dentin. These changes result in the activation of pulp receptors, such as baroreceptors and mechanoreceptors, and the subsequent activation of pain fibers, namely A-delta fibers, located in the pulpal wall. This mechanism can also occur through indirect stimulation of the odontoblasts [20,35-38].

From this viewpoint, when the hydrogen peroxide used in whitening procedures comes in contact with the dental structure and saliva, it reacts and produces free radicals [11]. These low-molecular-weight molecules can be dispersed through pores in the enamel and dentinal tubules, leaving them open and establishing direct contact with the pulpal tissue [20-22]. This process results in dehydration and fluid movement in the dentinal tubules and stimulation of the nerve endings [20].

The level of penetration of the bleaching agents through the dental structure and their consequent ability to reach the pulp can be influenced by many factors, such as the thickness of the enamel and dentin, structural changes, and the concentration of the whitening gel [39,40]. Teeth with thicker enamel and dentin function as a kind of barrier, offering the pulp greater protection [39]. Similarly, low concentrations of hydrogen peroxide do not penetrate as deep into the dentin [41].

### Inflammation from the bleaching procedure

The painful sensation of dental sensitivity can come from various stimuli, such as heat. However, as Haywood et al. (2005) [42] reported, most patients complain of tingling or widespread pain without a stimulus to set it off. Another aspect of dentin hypersensitivity is the presence of pain in intact teeth without exposed dentin [43]. In this case, we believe that changes to the pulp from the bleaching process are directly associated with the ability of the whitening agent to reach the pulpal bed because of its penetration into dental tissues, with pulpal inflammation being the result of this percolation [44,45].

Damage to the pulp tissues caused by tooth whitening can lead to the release of factors derived from cells, such as adenosine triphosphate [46] and prostaglandins, which excite or sensitize the pulpal nociceptors [47]. Charakorn et al. (2009) [48] have confirmed this finding, reporting that inflammatory mediators can sensitize or depolarize the nociceptors that innervate the pulp tissue. The released inflammatory mediators are eicosanoids - bioactive lipid mediators derived from the polyunsaturated arachidonic acid, due to the action of the cytosolic phospholipase A2 enzyme (PLA2) in the membrane phospholipids. PLA2 is regulated in response to mitogenic or inflammatory stimuli, as studies by Poczobutt et al. (2013) [49] have shown.

Arachidonic acid can be metabolized by two large classes of enzymes, cyclooxygenase (COX) and lipoxygenase. COX is responsible for the formation of various prostaglandins and thromboxanes. According to Li et al. (2011) [50], COX-2 is an enzyme induced by inflammatory stimuli that generate prostaglandins. Production of COX-2 would contribute to inflammation and pain [49]. This finding corroborates a study by Kamei et al. (2004) [51], which implicated prostaglandins in a series of physiological events, including the progression of inflammation and immunomodulation, as well as pain transmission. Thus, these substances play a critical role in the pathogenesis of pulp disease.

The inflammation of the tooth pulp is a complex process that involves both neural and vascular reactions and can cause reversible or irreversible pulpal changes. Neuropeptides are an important neural component that are present in the sensitive afferent neurons of the trigeminal and ganglia in the sympathetic fibers of the cervical ganglia [52]. The most important of these neuropeptides is Substance P, which is responsible for histamine release inside mastocytes, the induction of vasodilatation, the increase of pulpal blood flow, and, consequently, a more rapid and wider access by inflammatory cells and mediators to the inflammation site. This process can generate an inflammatory response and induce apoptosis of pulp cells, such as fibroblasts and undifferentiated mesenchymal cells [52].

### Advances in the use of medication to reduce transoperative dentin hypersensitivity

One of the biggest goals in tooth whitening research is reducing dentin hypersensitivity. Therefore, many studies have examined mechanisms to reduce this side effect. These studies have resulted in the development of desensitizing agents made of potassium or fluoride nitrate [48]. These agents are used before or after bleaching and can reduce dentin hypersensitivity during the whitening procedure [6]. They act by reducing the nerves' ability to respond to changes in the dentinal fluids, and reducing changes to the fluids caused by stimuli by reducing dentine permeability [53]. However, despite their relative effectiveness, desensitizing agents add a step to the clinical protocol, while most dental professionals are looking to simply the clinical procedure [6].

Another current method that has been extensively researched is the use of anti-inflammatory medication before and after the tooth whitening procedure [6,43,48]. The potential for anti-inflammatory agents to reduce hypersensitivity is supported by the theory that bleaching agents generate pulp inflammation, one of the factors responsible for this side effect. Anti-inflammatories, as their name suggests, act to modulate inflammation and pain. They act by blocking COX, thereby suppressing the production of prostaglandins, which are mediators released in response to tissue damage. Inhibiting these mediators guarantees the effectiveness of these compounds [24,54]. This group includes drugs such as ibuprofen, diclofenac, and naproxen [24].

Ibuprofen is classified as a non-steroidal anti-inflammatory, non-selective COX-2 inhibitor [24]. Various studies have evaluated its ability to decrease sensitivity from whitening procedures [6,48]. De Paula et al. [6] evaluated the pre-operative use of 400 mg of ibuprofen for a 48-hour period after bleaching. When ibuprofen was used starting one hour before the whitening treatment, it reduced the sensitivity during and immediately after the procedure, for a maximum of 1 hour. However, when analyzing the period between 1 hour and 24 hours after the procedure, there were no significant differences in terms of the intensity or incidence of dental sensitivity between the ibuprofen group and the control group. Using the medication did not affect the effectiveness of the tooth whitening agents.

In another study, De Paula et al. [43] evaluated the effect of a COX-2 selective anti-inflammatory (etoricoxib 60 mg), on dentin hypersensitivity from bleaching. The drug was administered one hour before the procedure and 24 hours afterwards.

Unexpectedly, etoricoxib was unable to reduce dentin hypersensitivity. There are two possible explanations for this result. One possibility is that the COX-2 expression in the pulp of the recently whitened teeth was low. Another possibility is that etoricoxib was not effective on all of the inflammatory mediators related to the pulpal inflammation causing the bleaching-related sensitivity [43].

## CONCLUSIONS

Of the anti-inflammatory medications tested, only ibuprofen seemed to show a relationship with the reduction of dentin hypersensitivity. More studies are needed to suggest a method or medication that can effectively reduce the dentin hypersensitivity associated with tooth whitening.

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