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**Clinical Research**

# The Effect of Preoperative Ibuprofen on Tooth Sensitivity Caused by In-office Bleaching

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### Clinical Relevance

The use of an analgesic may help to reduce tooth sensitivity during in-office bleaching. Within the limitations of this study, Ibuprofen (600 mg, PO single dose) reduced tooth sensitivity during, but not after the treatment period.

## SUMMARY

**This study determined the effect of Ibuprofen on tooth sensitivity from in-office bleaching with 38% hydrogen peroxide. A double-blind, randomized-controlled clinical trial was performed on healthy non-smoker patients who retain all anterior teeth (N=31). Patients with anterior restorations, calculus or heavy stain, and those who were taking medications or desensitizer products were excluded. After signing the informed consent, the patients were randomly divided into a Placebo group (n=16) that received a placebo (tinted oil in clear capsule) (Health Dimensions Inc, Compound Pharmacy, Farmington Hills, MI, USA) or an Ibuprofen group (n=15) that received a 600 mg, PO single dose of Ibuprofen (Advil Liquid Gel, Wyeth, Madison, NJ, USA). The patients were watched while taking the capsules 30 minutes prior to treatment. A single operator applied the 38% hydrogen peroxide (Opalescence Xtra Boost, Ultradent Products Inc) for 20 minutes on 12 anterior teeth. The hydrogen peroxide solution was then rinsed, the teeth were gently dried and the cycle was repeated, for a total application time of 40 minutes. A Visual Analog Scale (VAS) was used to evaluate the level of sensitivity 30 minutes before treatment, immediately after treatment, then 1 hour and 24 hours post-bleaching. The patients graded their maximum sensi-**

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**tivity levels during each period on a scale from 0 to 100 (0=no sensitivity, 100=unbearable sensitivity). The VAS scores were statistically analyzed to compare the groups' scores at different times and to compare the scores within each group at various times (Wilcoxon rank sum tests). The mean score and standard deviation of the Ibuprofen group immediately after bleaching was 5.0 ± 9.9, at 1 hour—31.5 ± 32.1 and at 24 hours—25.8 ± 30.8; the placebo group at the time of treatment was 26.6 ± 31.0, at 1 hour—30.9 ± 30.5 and at 24 hours—31.1 ± 32.6. When comparing the two groups at different times, the Ibuprofen group showed statistically significantly lower sensitivity scores immediately post-bleaching than the placebo group ($p$=0.0216) but not at 1 hour ($p$=0.84) or 24 hours post-bleaching ($p$=0.54). When comparing times within the Ibuprofen group, the mean VAS score immediately after bleaching was significantly lower than 1 hour post-bleaching ($p$=0.0024) and 24-hours post-bleaching ($p$=0.0110), but the mean VAS score at 1 hour post-bleaching and 24-hours post-bleaching were not significantly different ($p$=0.64). For the placebo group, the intragroup time effect was not significant. Within the limitations of the current study, the authors concluded that the use of an analgesic may help to reduce tooth sensitivity during in-office bleaching. In the current study, Ibuprofen (600 mg, PO single dose) reduced tooth sensitivity during but not after the treatment period.**

## INTRODUCTION

Odontogenic pain is usually caused by either noxious physical stimuli or the release of inflammatory mediators. The most widely accepted theory that explains tooth sensitivity is the hydrodynamic theory. This theory postulates that the rapid movement of fluids within the dentinal tubules, following stimulus application, results in activation of sensory nerves in the pulp or inner dentin region of the tooth. Physical stimuli can activate the nociceptors that innervate dentinal tubules, leading to the perception of dental pain. Inflammatory mediators can sensitize or depolarize the nociceptors that innervate pulpal tissue. The process involves two major classes of enzymes: cyclooxygenases (COX) and lipoxygenases. The COX pathway leads to the generation of prostaglandins, which have been known to play a critical role in the pathogenesis of pulpal disease. The direct involvement of prostanoids in pulpal pain was proposed when the intravenous administration of non-steriodal anti-inflammatory drugs (NSAIDs), which are known to block the COX pathway, resulted in the significant inhibition of stimulated nerve activity in cat pulp.[1]

Tooth discoloration varies in etiology, appearance, localization, severity and level of adherence to tooth structure. After tooth eruption, aging and pulp necrosis are the main causes of intrinsic discoloration. Coffee, tea, red wine, carrots, oranges and tobacco can give rise to extrinsic stain.[2-3] Although the scaling and polishing of teeth removes many extrinsic stains, the results may not be satisfactory. Vital tooth bleaching is a highly successful, non-invasive method to treat discolored teeth.[4] There are various methods of vital tooth bleaching, but the three basic fundamental approaches include dentist-supervised night guard bleaching, mass market bleaching products and in-office or power bleaching.[5]

Gingival irritation and tooth sensitivity are the most common side effects of vital tooth bleaching.[6] For example, one clinical study showed that 55% of patients treated with 10% carbamide peroxide reported tooth sensitivity, and 20% of those who experienced side effects terminated treatment due to discomfort.[7] Currently, the mechanisms of tooth sensitivity after external tooth bleaching have not yet been fully determined, but inflammatory mediators may play an important role. Some studies have attempted to evaluate pulpal histology after bleaching, but with contradictory results. Structural pulp damage was not observed in human premolars exposed to 35% hydrogen peroxide *in vivo*, which had been extracted and submitted for histological evaluation 30 days after exposure.[8] However, histologic evaluation of human pulp after overnight vital bleaching with 10% carbamide peroxide revealed mild inflammatory changes in four out of 12 teeth after both four and 14 days.[9]

Ibuprofen is an NSAID that is believed to work through the inhibition of cyclooxygenase (COX), thus inhibiting prostaglandin synthesis. There are at least two variants of cyclooxygenase (COX-1 and COX-2), and Ibuprofen inhibits both COX-1 and COX-2. It appears that Ibuprofen's analgesic, antipyretic and anti-inflammatory activity are achieved principally through COX-2 inhibition. This NSAID is currently widely used as pre-medication for in-office bleaching treatment in some dental practices, and unpublished data from a clinical experiment suggested that a combination of Ibuprofen and acetaminophen may decrease tooth sensitivity from in-office bleaching.[10] However, currently, no other studies support that regimen.

The current study determined the effect of Ibuprofen on tooth sensitivity associated with in-office bleaching with 38% hydrogen peroxide. The authors chose this in-office bleaching approach, because patients may suffer from sensitivity to cold and intermittent spontaneous pain lasting up to one day after treatment.[5] The results of the current study could support the use of pre-medication for in-office bleaching treatment and its routine use in clinics.

## METHODS AND MATERIALS

### Study Design and Subject Recruitment

A double-blinded randomized-control clinical trial was utilized to measure the level of tooth-sensitivity in patients by using a modified visual analog scale (VAS). The current study proposal was submitted and approved by the Institutional Review Board Committee of the University of Detroit Mercy. Thirty-three patients were screened and recruited from the School of Dentistry, University of Detroit Mercy, following the exclusion and inclusion criteria featured in Table 1. Each patient was asked to sign the informed consent form before beginning the experiment. The patients were randomly divided into two groups: the control group–patients who received a placebo (tinted oil in clear capsules) (Health Dimensions Inc, Compound Pharmacy, Farmington Hills, MI, USA), and the experimental group–patients who received a 600 mg, PO single dose of Ibuprofen (Advil Liquid Gel, Wyeth, Madison, NJ, USA). All the patients were watched to ensure that they took the analgesic drugs or placebo 30 minutes prior to treatment.

### In-office Bleaching Treatment Procedure

Each patient received an in-office bleaching treatment with 38% hydrogen peroxide (Opalescence Xtra Boost, Ultradent Products, Inc, South Jordan, UT, USA) following the instructions provided by the manufacturer. Cheek retractors (KleerView, Ultradent Products, Inc) and disposable tongue guards (IsoBlock, Ultradent Products, Inc) were used to isolate the lips, tongue and peripheral soft tissue from the bleaching area. The light-cured resin (OpalDam, Ultradent Products, Inc) was used to maintain a gingival barrier overlapping the teeth 2 mm from the free gingival margin or the cemento-enamel junction. The bleaching gel was applied on both the maxillary and mandibular anterior teeth and remained on the teeth for 20 minutes. The gel was then rinsed off and the teeth gently dried. Another cycle was repeated at the same sitting, providing a total of 40 minutes where the bleaching gel was in contact with the tooth surfaces. All the materials were applied by a single operator.

### Tooth-sensitivity Level Measurement

The effect of each analgesic was evaluated for 30 minutes prior to treatment, immediately after treatment (0 hour), 1 hour and 24 hours after the treatment was completed. The authors of the current study designed the VAS scores for tooth sensitivity so that zero indicated "no sensitivity" and the 100 mm end indicated "unbearable sensitivity." The patients were asked to grade their sensitivity, rating their maximum sensitivity levels perceived during each period. At the 24-hour recall appointment, the patients were interviewed regarding their experience.

### Statistical Analyses

The VAS scores were recorded by measuring the distance in millimeters from the zero point to the mark indicating the patients' relative sensitivity. The recorded scores were subtracted from the baseline, which was recorded at 30 minutes prior to treatment to standardize individual variation. The mean level and standard deviation of VAS scores were calculated. The data sets were plotted on histograms and inspected for normal distributions. Some data did not appear to be normally distributed and, therefore, non-parametric statistical tests were used to compare the various treatments. To further investigate distribution of the data, the skewness and kertosis were calculated and found to be much greater than the +2 to –2 standard errors of skewness and kertosis that would indicate normal distributions. Statistical analyses of mean VAS scores comparing the two groups at immediate post-bleaching, 1 hour and 24 hours post-bleaching were performed using the Wilcoxon rank sum tests. Comparisons between times within each group were performed using the Wilcoxon rank sum tests. Comparisons for sex differences between the two groups were performed using a Chi-square test, and for age differences, the Wilcoxon rank sum tests were used. In all statistical tests, the significance level was $\alpha$=0.05. *P*-values less than or equal to 0.05 indicated significant differences.

Table 1: *Inclusion and Exclusion Criteria*

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| 1. Candidates must have all six anterior maxillary and six anterior mandibular teeth. | 1. Candidates with a history of any medical disease that may interfere with the study or require special considerations. |
| 2. Those teeth must not have restoration involved labial surface or labially pass the contact area from the lingual surface. | 2. Candidates who have used tobacco products during the past 30 days. |
| 3. Candidates must be willing to sign a consent form. | 3. Candidates who have gross pathology in the oral cavity. |
| 4. Candidates must be at least 18 years of age. | 4. Candidates who are pregnant or lactating. |
| 5. Candidates must be able to return for periodic examinations. | 5. Candidates who have calculus or heavy stain on the study sites. |
| 6. Candidates must be non-smokers. | 6. Candidates who have a history of sensitivity or adverse reactions to ibuprofen or NSAID. |
| | 7. Candidates who recently or currently use drugs, alcohol or over-the-counter pain relievers. |
| | 8. Candidates who recently or currently use desensitizer toothpaste or over-the-counter desensitizer products. |

## RESULTS

The data from 31 patients were used in this study. (Two patients were excluded from the study due to leakage of the bleaching gel into the gingival tissue during treatment.)

When comparing the two groups, the Ibuprofen group showed a statistically significant lower mean VAS score immediately after bleaching, compared with the placebo group ($p$=0.0216). Both groups did not have statistically significant differences one hour post-bleaching ($p$=0.84) or 24-hours post-bleaching ($p$=0.54).

When comparing times within treatment groups, the Ibuprofen group's mean VAS score immediately after bleaching was significantly lower than the one hour post-bleaching ($p$=0.0024) and 24 hours post-bleaching ($p$=0.0110), but the mean VAS scores at one hour post-bleaching and 24 hours post-bleaching were not significantly different ($p$=0.64). For the placebo group, the difference between times was not significant: Mean VAS scores immediately after bleaching and one hour post-bleaching ($p$=0.77), immediately after bleaching and 24 hours post-bleaching ($p$=0.40), and one hour post-bleaching and 24 hours post-bleaching were not significantly different ($p$=0.79) (Figure 1 and Table 2).

The two groups were not significantly different with respect to sex ($p$=0.85) or age ($p$=0.37) (Table 3A and 3B).

At the 24-hour recall appointment interview, most patients described their sensitivity as "shock-like" or "twinging" pain, with varied frequency and intensity.

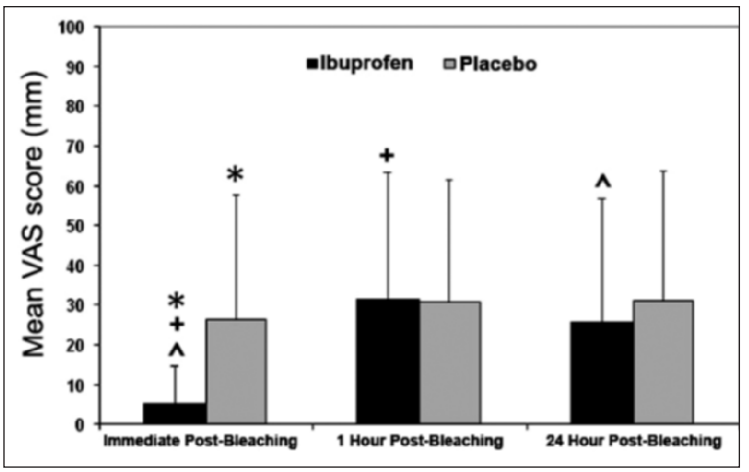


Figure 1. *Comparisons of the mean VAS score (mm) of the Ibuprofen group versus the placebo group at different times. Note: (*) indicates significant differences between the Ibuprofen and Placebo groups at immediate post-bleaching (p<0.05). (+) indicates significant differences between the immediate post-bleaching and one hour post-bleaching within the Ibuprofen group (p<0.05). (^) indicates significant differences between immediate post-bleaching and 24 hours post-bleaching within the Ibuprofen group (p<0.05).*

Table 2: *Data of the Mean VAS Score of Sensitivity Level During In-office Bleaching in Different Time*

| Time | Group | VAS (mm) Mean | Min | Max |
|---|---|---|---|---|
| Immediate | Ibuprofen | 5.0 ± 9.9 | 0 | 38 |
| | Placebo | 26.6 ± 31.0 | 0 | 85 |
| 1 Hour Post-bleaching | Ibuprofen | 31.5 ± 32.1 | 0 | 92 |
| | Placebo | 30.9 ± 30.5 | 0 | 83 |
| 24 Hours Post-bleaching | Ibuprofen | 25.8 ± 30.8 | 0 | 100 |
| | Placebo | 31.1 ± 32.6 | 0 | 96 |

Table 3A: *Sex Distribution of Patients*

| Group | N | Female | Male |
|---|---|---|---|
| All | 31 | 15 (48%) | 16 (52%) |
| Ibuprofen | 15 | 7 (47%) | 8 (53%) |
| Placebo | 16 | 8 (50%) | 8 (50%) |

## DISCUSSION

### Observation

In the current study, the authors observed that Ibuprofen (600 mg, PO single dose) decreased tooth sensitivity associated with in-office bleaching only during treatment time. This finding suggests that Ibuprofen (600 mg, PO single dose) may be used to help patients who have a lower pain threshold get through the treatment. Some patients reported that they had "severe shock-like pain" within one hour after treatment. The peak time range where patients experienced the most sensitivity was between one and six hours after treatment. This may be explained by the decreasing amount of Ibuprofen in patients' serum as time passes. The half-life elimination of Ibuprofen is two-to-

Table 3B: *Age Distribution of Patients*

| Group | Frequency of Age Distribution (N) 20-29 years old | 30-41 years old | Total | Age (years old) Mean+SD | Min | Max |
|---|---|---|---|---|---|---|
| All | 27 | 4 | 31 | 25.0 ± 4.2 | 20 | 41 |
| Ibuprofen | 14 | 1 | 15 | 25.1 ± 3.0 | 20 | 30 |
| Placebo | 13 | 3 | 16 | 24.9 ± 5.2 | 21 | 41 |

four hours, thus, a second dose may be required to keep the Ibuprofen serum level sufficiently high for optimum analgesic effect. Further investigations are needed to determine the optimum dosing schedule.

### Study Limitations

One of the limitations of the current study could be the variation in tooth structure thickness between patients. The amount of bleaching agent that penetrates through the tooth structure is influenced by enamel and dentin thickness.[11] The authors of the current study assumed that their sample group would represent the general population, despite the fact that most of the people who had fixed orthodontic appliances might have received slight enamel adjustments that could have affected the results of the study.

Furthermore, the use of VAS is controversial, because it is considered a highly subjective measurement technique. However, this scale has been used for pain measurement in numerous studies. In the current study, each subject's pain threshold limited the accuracy of the result. Some patients experienced no sensitivity from the bleaching treatment. Future studies should be conducted with a larger sample size to limit this variation.

## CONCLUSIONS

The use of an analgesic may help to reduce tooth sensitivity during in-office bleaching treatment. Ibuprofen (600 mg, PO single dose) reduced tooth sensitivity during the treatment period. Further studies are necessary to confirm this finding and to investigate the dosage for optimal effect.

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