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Preemptive Use of Naproxen on Tooth Sensitivity Caused by In-Office Bleaching: A Triple-Blind, Crossover, Randomized Clinical Trial

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Clinical Relevance

The administration of single-dose naproxen to prevent tooth sensitivity caused by in-office bleaching had limited effectiveness.

SUMMARY

Objectives: A triple-blind, randomized, crossover clinical trial evaluated prior use of non-steroidal anti-inflammatory naproxen on sensitivity reported by patients undergoing in-office tooth bleaching.

Methods and Materials: Fifty patients were subjected to two sessions of in-office tooth bleaching with 35% hydrogen peroxide in a single application of 40 minutes for two sessions, with an interval of seven days between applications. One hour prior to the procedure, each patient randomly received a single dose of naproxen (500 mg) or placebo. The patient's sensitivity level was evaluated during and immediately after the bleaching using two scales (verbal and visual analog); the verbal scale only was repeated after 24 hours. The effectiveness of the bleaching procedures was evaluated with the Bleachedguide scale. Relative risk to sensitivity was calculated and adjusted by session, while comparison of overall risk was performed by the McNemar test. Data on the sensitivity level for both scales and shade were subjected to the Friedman, Wilcoxon, and Mann-Whitney tests (α=0.05).

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Results: The use of naproxen only decreased the absolute risk and intensity of tooth sensitivity reported immediately after the second session. On the other hand, no measurable effect was observed during or 24 hours after either session. The sequence of drug administration did not affect the bleaching effectiveness.

Conclusions: Preemptive use of naproxen only reduced tooth sensitivity reported by patients immediately after the second session of bleaching.

INTRODUCTION

Tooth bleaching is a noninvasive procedure used with great success to treat teeth with color alteration that compromises esthetics.[1-4] Among the techniques used for bleaching vital teeth, the technique performed in-office is usually indicated for certain clinical conditions, including for patients presenting with a contraindication for using the at-home technique (such as those with gastrointestinal disorders) or those who prefer not to use bleaching trays.[5-7] The in-office techniques are performed using high concentration hydrogen peroxide (H_2O_2) for a shortened exposure time compared to the time needed to perform the technique at home. The H_2O_2 radicals are responsible for whitening the tooth; however, these radicals are also able to diffuse through the dentin and reach the dental pulp, resulting in inflammatory reactions of this tissue.[8-10]

The presence of these components generates oxidative reactions that release inflammatory chemical mediators and induce cellular apoptosis.[11,12] Clinically, these reactions result in tooth sensitivity during and after the bleaching process, which is the main adverse effect associated with this procedure. Clinical trials have reported elevated absolute risk of developing tooth sensitivity during and after in-office bleaching, as more than 90% of patients subjected to the procedure report sensitivity.[2-4] Sensitivity reported by patients is transient and disappears a few hours after the procedure; however, the presence of tooth sensitivity can impair the continuity of treatment and compromise its results.[13,14]

Considering the high rate of tooth sensitivity reported by patients, several approaches have been evaluated that are aimed at reducing the sensitivity caused by dental bleaching, including the use of desensitizing agents[15-18] or antioxidants[19] prior to the bleaching procedure. However, these protocols increase the number of operatory steps, and clinicians prefer to limit the use of time-consuming protocols. The preemptive use of anti-inflammatories has also been attempted, but the drugs that have been evaluated were unable to prevent or reduce postbleaching sensitivity.[20-23] The limited action of these anti-inflammatories on bradykinin and substance P, which are important mediators of pain caused by tooth bleaching,[24,25] can be related to the absence of favorable outcomes in previous trials.[20-23] A common anti-inflammatory drug acting on these mediators is naproxen, which can help control tooth sensitivity.[26] Naproxen sodium is a propionic acid derivative that inhibits the cyclooxygenase pathway, thus preventing the release of inflammatory mediators, such as prostaglandins and bradykinin.[27] Further, naproxen is an effective treatment for postoperative pain when administered in a single dose,[26-28] while this drugs reaches its peak of plasma concentration two to four hours after the oral administration.[29]

The effectiveness of naproxen on bradykinin and its pharmacokinetics motivated this study to evaluate whether this drug may be effective in the prevention of tooth sensitivity caused by in-office bleaching. Thus, this randomized controlled clinical trial aimed to evaluate the effectiveness of preemptive prescription naproxen versus placebo on the absolute risk of postoperative tooth sensitivity (primary outcome) associated with in-office bleaching. The hypothesis was that administrating a single dose of naproxen prior to an in-office bleaching procedure would reduce the absolute risk of postoperative tooth sensitivity. The intensity of tooth sensitivity and color evaluation, both secondary outcomes, were also evaluated.

METHODS AND MATERIALS

This clinical trial was approved by the scientific review committee and by the committee for the protection of human subjects of the local university (CAAE: 37578714.4.0000.5546). The protocol of study was registered at https://clinicaltrials.gov under number NCT02463552 and followed the CONSORT statements.

Study Design

This study was a randomized, triple-blind, placebo-controlled clinical trial with a crossover design. The patients included were submitted to two in-office bleaching sessions, receiving a placebo (control) or naproxen prior to the bleaching procedure, while different treatments were allocated for each session.

A delay of one week between the session ("washout") was established. The study was conducted at the school of dentistry of the local university from November 2014 to July 2015.

Inclusion and Exclusion Criteria

Patients included in the study were at least 18 years old and in good general and oral health. Participants were recruited by advertisements attached to boards located on university buildings. Patients with caries, restoration, severe discoloration (eg, stains caused by tetracycline), enamel hypoplasia, gingival recession, dentin exposure, cracks visible on buccal enamel, pulpitis, or endodontics on any of the six upper anterior teeth were excluded. Participants who had undergone a previous bleaching procedure, presented prior tooth sensitivity, had a known allergy to any component of the medication used in the study, were under continuous use of anti-inflammatory or analgesic drugs, smoked, had parafunctional habits, were using oral removable or fixed orthodontic appliances, or were pregnant or breast-feeding were excluded. The tooth shade of eligible participants was evaluated using the VITA Bleachedguide 3D-MASTER (Vita-Zahnfabrik, Bad Sackingen, Germany) scale, and only the participants presenting all six upper anterior teeth matched to the shade 2.5 M2 or the darker tab of this scale were included. Following color evaluation, a slight airstream was applied over the buccal surfaces of the upper maxillary teeth; patients reporting any tooth sensitivity at this time were excluded.

Sample Size Calculation

The sample size calculation was based on primary outcome data (absolute risk measured immediately after the procedure) from a previous study using a similar bleaching protocol.[20] The calculation was performed for a superiority trial with a binary outcome, considering a power test of 80%, a significance level of 5%, and a decrease of 30% for the experimental treatment compared to the control in a crossover design. Thus, 48 patients were required, and 50 patients were included in the randomization to address the possibility of dropout during the follow-up.

Random Sequence Generation and Allocation Concealment

A randomized list was computer generated by a person not involved in the intervention or evaluation. The participants were defined as a block in the randomization process, and the sequence of treatment (placebo or naproxen) was randomly set for each block by using computer-generated tables. The sequence was inserted into sealed envelopes numbered from 1 to 50 that were opened by the operator only at the moment of the intervention. The patients were numbered according to the sequence of enrollment. Neither the participant nor the operator knew the group allocation determining blinding to the protocol.

Baseline Measurements

Two evaluators were previously calibrated to assess tooth shade using the Bleachedguide scale. The agreement evaluation was performed by analyzing the shade of the upper teeth of six patients not included in the study two times, with a three-day interval between. The kappa coefficient was used to calculate for intraevaluator (evaluator 1=0.80; evaluator 2=1.00) and interevaluator (0.70) agreement. Thus, the calibrated evaluators evaluated the shade of the anterior upper teeth prior to the bleaching procedure based on a match of color between the scale tabs and the middle third of the tooth crown. The shade tabs selected were converted to scores ranging from 1 (whiter shade—0 M1) to 15 (darker shade—5 M3). Considering a possible effect of dental anxiety of sensitivity reported by patients, the Corah Dental Anxiety Scale was used to determine each patient's level of anxiety related to the procedure.[30] Each answer to the survey instrument was scored on a scale from 1 to 5 (four questions), and the sum of the scores was used to determine the level of anxiety: low—lower than 12, moderate—between 12 and 14, and high—higher than 14.

Intervention

Identical capsules containing either 500 mg of naproxen or placebo (inert content) were manufactured by the local university's pharmacy department. The capsules were manufactured by individuals not involved in the intervention or evaluation and were placed into two bottles identified by letters according to the treatment. Neither the researchers responsible for the intervention and evaluation nor the patients knew the content of each capsule. One hour prior to the in-office bleaching procedure, the patient received a single dose of a capsule containing naproxen or placebo. Dental prophylaxis was performed with pumice and water using a rubber cup, and a light-polymerized resin dam (Top Dam, FGM, Joinville, Brazil) was applied over the gingival tissue corresponding to the teeth to

be bleached. A 35% hydrogen-peroxide–based whitening agent (Whiteness HP Blue, FGM) was used according to the manufacturer's recommendation but without the prior application of desensitizing topical to not affect the evaluations of tooth sensitivity. The whitening agent was applied over the buccal surfaces of the teeth and remained in position for 40 minutes, while any bubbles from oxygen release were released with the aid of a disposable microapplicator. After the peroxide removal, the enamel was polished with felt disks. A second session of bleaching was performed after one week, during which time the patient received the opposite treatment (naproxen or placebo) from the one received prior to the first session.

Evaluations

The tooth sensitivity reported by patients was recorded using both a visual analog scale (VAS) and a verbal rating scale (VRS). For the VAS, the patient set his or her sensitivity level by pointing with a pen to the colored 10-cm scale, which ranged from green (no pain) to red (extreme pain). The distance between the marking and the green border of the scale was recorded. Tooth sensitivity was also scored according to VRS, where 0 = none, 1 = mild, 2 = moderate, 3 = considerable, and 4 = severe. Tooth sensitivity was evaluated during the bleaching procedure and immediately after bleaching agent removal. Tooth sensitivity was recorded again 24 hours after the procedure using only the VRS. The VRS defined the presence (score different from 0) or absence of tooth sensitivity in all time assessments. This binary outcome (main outcome) was used to define the risk to tooth sensitivity. A new shade evaluation of the six anterior maxillary teeth was performed one week after each bleaching session. All evaluations were performed by two evaluators blinded to the allocation assignment.

Statistical Analysis

The analysis followed the intention-to-treat protocol and involved all the participants, who were randomly assigned. The statistician was blinded to the study groups. Data from each patient's profile were analyzed regarding distribution of age, gender, and level of anxiety for each sequence of treatment. Age data were analyzed by the Mann-Whitney rank sum test due to the absence of normal distribution (Kolmogorov-Smirnov, $p<0.05$). The proportions of each gender and level of anxiety were analyzed by the Fisher exact and chi-square tests, respectively.

Based on the presence of any tooth sensitivity (scores different from 0 at VRS), the absolute risk, the odds ratio, and the relative risk, as well as confidence intervals (95%), were calculated for each treatment for each evaluation/session of bleaching. For each session, differences in the presence/absence ratios were analyzed by the Fisher exact test. For the overall risk related to each treatment, the odds ratio was adjusted to the independent variable "session of bleaching" using the Mantel-Haenszel statistic. The homogeneity of the odds ratio was analyzed by the Breslow-Day and Tarone tests. Then the estimated odds ratio was converted to relative risk, and the overall presence/absence ratios were analyzed by the McNemar test, considering the study design (crossover).

For both scales of tooth sensitivity evaluation, the data from the scores observed in each evaluation/session of bleaching were subjected to a Mann-Whitney rank sum test. The average scores for each treatment were compared using a Wilcoxon signed rank test.

For color evaluation, comparisons were performed among the sequences of treatment. Changes in the number of shade guide units (ΔSGU) were calculated from baseline to express the color alteration. Data were submitted to two-way repeated measures analysis of variance. All statistical analyses were performed considering a significance level of 95%.

RESULTS

The participants' flow diagram in the different phases of the study is shown in Figure 1. One hundred fifty-two patients were excluded during the enrollment due to presence of prior tooth sensitivity, restorations, teeth previously bleached, or whiter than 2M2 in order to not affect the outcomes measurements. None of the patients discontinued the intervention or presented adverse effects during the intervention. Demographic data from patients included in the study are displayed in Table 1. The age of the included patients presented a median of 23 years and no significant difference was observed between the patients allocated for each sequence of treatment. Both sequences of allocation presented the same distribution as related to gender with a predominance of females (64.0%). For both sequences of treatment, most patients included in the study demonstrated low anxiety (82.0%) to tooth bleaching.

The results of risk to tooth sensitivity are presented in Table 2. The treatment received by

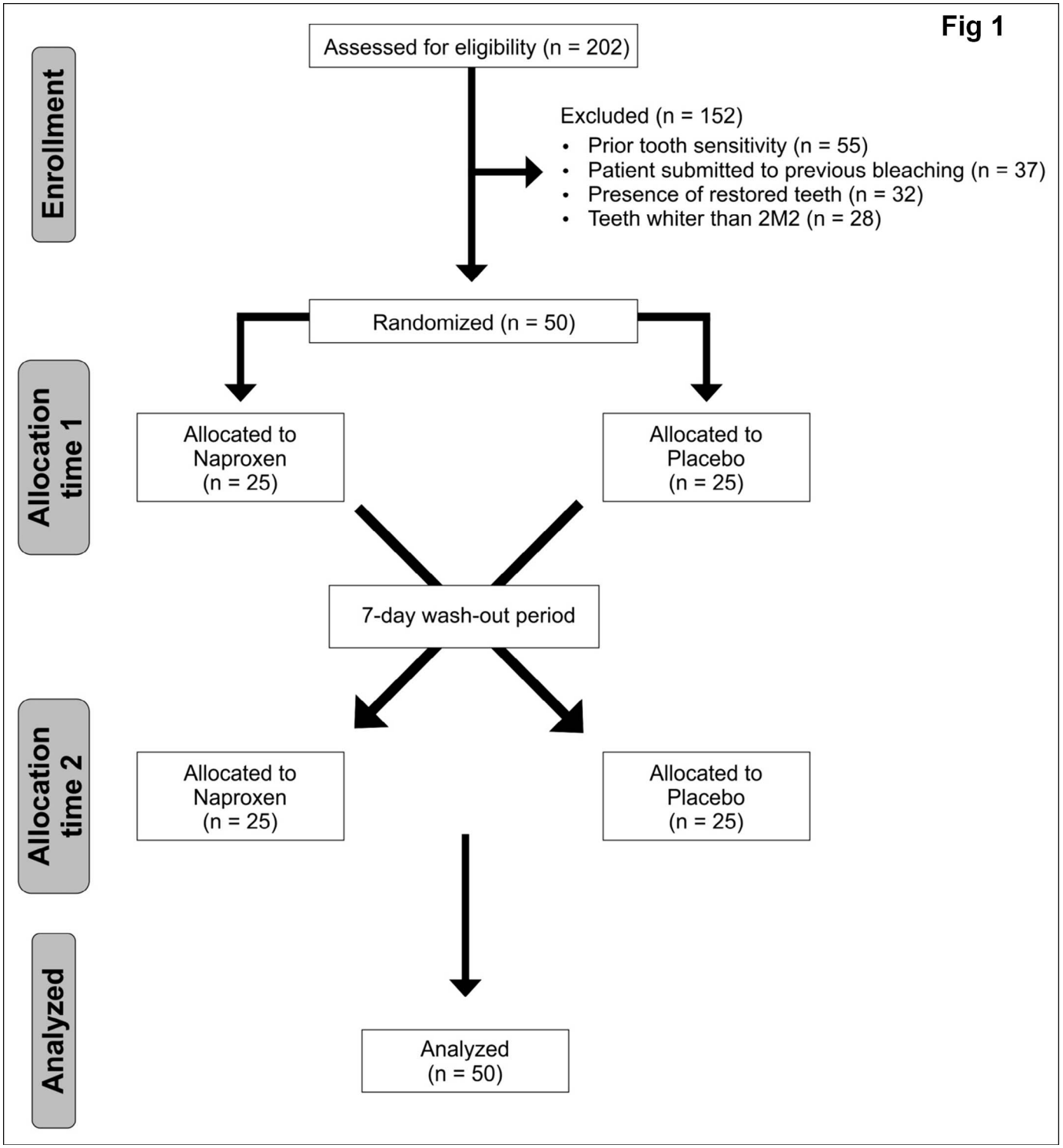

Figure 1. *Flow diagram of the clinical trial.*

the patient did not affect the risk of tooth sensitivity caused by bleaching for the evaluations performed during the procedure or after 24 hours. On the other hand, the use of naproxen reduced the risk of tooth sensitivity in 57% of patients when measured immediately after the second session of bleaching. The same effect was not observed in the first session of tooth bleaching.

Table 1: *Baseline Demographic Characteristics of the Study Population*

Age (y)	Median (First/Third Quartiles)	
Total	23 (21/26)	
Placebo/naproxen	23 (21/26)	$p = 0.883$[a]
Naproxen/placebo	23 (22/26)	
Gender		
Total	Number (%)	
Male	18 (36.0%)	
Female	32 (64.0%)	
Placebo/naproxen		
Male	9 (36.0%)	
Female	16 (64.0%)	$p = 1.000$[b]
Naproxen/placebo		
Male	9 (36.0%)	
Female	16 (64.0%)	
Level of anxiety	Proportion (%)	
Total		
Low anxiety	41 (82.0%)	
Moderate anxiety	6 (12.0%)	
High anxiety	3 (6.0%)	
Placebo/naproxen		
Low anxiety	21 (84.0%)	
Moderate anxiety	3 (12.0%)	
High anxiety	1 (4.0%)	$p = 0.836$[c]
Naproxen/placebo		
Low anxiety	20 (80.0%)	
Moderate anxiety	3 (12.0%)	
High anxiety	2 (8.0%)	

[a] *Mann-Whitney rank sum test.*
[b] *Fisher exact test.*
[c] *Chi-square test.*

Regarding the level of sensitivity, results from the VRS and the VAS are presented in Tables 3 and 4, respectively. At evaluations performed during the tooth bleaching and after 24 hours (only for the VRS), treatment did not affect the level of sensitivity. However, a lower level of tooth sensitivity was observed in patients who received naproxen in the evaluation performed immediately after the second session regardless of the scale used. During the second session, only the VAS demonstrated reduced tooth sensitivity for the patients who received naproxen. On the other hand, no effect of preemptive use of naproxen was observed after the first session.

The results of color evaluation are presented in Table 5. Two-way repeated measures analysis of variance showed a significant effect only for the moment of evaluation ($p<0.001$), whereas the sequence of allocation ($p=0.590$) and the interaction ($p=0.057$) were not significant. Regardless of the sequence of allocation, higher values of ΔSGU were observed after the second session of tooth bleaching.

DISCUSSION

Despite the cytoplasmic extensions of the odontoblasts, dentinal fluid, and enzymes from pulp tissue to hinder peroxide penetration through the pulp chamber, it is common for patients submitted to in-office bleaching to report postoperative tooth sensitivity.[2-4,8,13] This sensitivity is related to inflammatory processes induced by the presence of peroxide and its products in pulp tissue, resulting in a reduction of cell proliferation, metabolism, viability, pulp-reparative capacity, and pain.[11] Inflammatory processes are extremely complex, and several mediators of pain and inflammation are released by host cells in response to specific stimuli. Thus, oxidative stress caused by peroxide penetration into the pulp chamber increases the level of mediators of inflammation such as prostaglandins, bradykinin, and substance P.[24,25,31] Among these mediators, the presence of bradykinin was seen in the inflammatory process in pulp tissue, and this nonapeptide plays a pivotal role in the production of pain.[32]

In the present study, nonsteroidal anti-inflammatory naproxen was preemptively administered to reduce the risk of postoperative tooth sensitivity caused by in-office bleaching. Interestingly, preemptive naproxen administration was only effective in reducing tooth sensitivity (both risk and level) reported at the second bleaching session, mainly the sensitivity measured immediately after the last session. Thus, the hypothesis of study was rejected. One important observation was that only VAS showed a reduction of tooth sensitivity with naproxen when the evaluation was carried out during the second bleaching procedure. Contrary to the VRS, which uses discrete data (score), continuous data are obtained with the VAS, allowing higher sensitivity to measure slight differences.

In addition to peroxide concentration, the number of exposures of pulp tissue to a bleaching agent is closely related to the inflammatory response.[33-35] Therefore, an increased level of inflammatory mediators can be expected after the second session compared to that observed after the first session. It was demonstrated that the action of naproxen over bradykinin depends on the presence of prostaglandins;[27] thus, it was speculated that a higher level of pulp inflammation after the second session increased the effectiveness of naproxen to reduce tooth sensitivity. However, even in the second session, using

Table 2: *Results for Risk to Tooth Sensitivity Observed for Each Treatment*

Session	Moment of Evaluation	During		Immediately After		24 h After	
	Treatment	Naproxen	Placebo	Naproxen	Placebo	Naproxen	Placebo
First session	Presence of sensitivity (yes/no)	14/11	10/15	10/15	9/16	4/21	1/24
	Absolute risk (95% CI)	0.56 (0.37-0.73)	0.40 (0.23-0.59)	0.40 (0.23-0.59)	0.36 (0.20-0.56)	0.16 (0.06-0.35)	0.04 (0.01-0.20)
	Odds ratio (95% CI)	1.91 (0.62-5.88)		1.19 (0.38-3.72)		4.58 (0.47-44.17)	
	Relative risk (95% CI)	1.27 (0.73-2.23)		1.11 (0.55-2.26)		4.00 (0.48-33.33)	
	p-value[a]	0.396		1.000		0.349	
Second session	Presence of sensitivity (yes/no)	9/16	14/11	6/19	14/11	1/24	4/21
	Absolute risk (95% CI)	0.36 (0.20-0.56)	0.56 (0.37-0.73)	0.24 (0.12-0.43)	0.56 (0.37-0.73)	0.04 (0.01-0.20)	0.16 (0.06-0.35)
	Odds ratio (95% CI)	0.44 (0.14-1.38)		0.25 (0.07-0.83)		0.22 (0.02-2.11)	
	Relative risk (95% CI)	0.64 (0.34-1.20)		0.43 (0.20-0.93)		0.25 (0.03-2.08)	
	p-value[a]	0.256		0.042		0.349	
Average	Odds ratio (95% CI)[b]	0.93 (0.43-2.01)		0.56 (0.25-1.25)		1.00 (0.28-3.60)	
	Relative risk[c]	0.96		0.70		1.00	
	p-value[d]	0.789		0.264		0.617	

Abbreviation: CI, confidence interval.
[a] *Fisher exact test.*
[b] *Mantel-Haenszel common odds ratio estimate.*
[c] *Based on odds ratio, estimated.*
[d] *McNemar test.*

preemptive naproxen did not affect the risk of tooth sensitivity reported by patients during the bleaching procedure and after 24 hours, while a reduced effect on sensitivity was observed during the procedure. These outcomes are related to the pharmacokinetics of naproxen after oral administration. Oral naproxen reaches its peak of plasma concentration after two to four hours.[29] Therefore, considering the methodology used in the present study, the plasma concentration of naproxen was reached during or a few minutes after the bleaching procedure. The study design with preemptive treatment administered one hour prior to the bleaching procedure was defined based on clinical protocols to prevent postoperative pain using a single dose of drug.[36,37] However, the findings of the present study suggest that this time delay might not be enough to allow more effective action of some anti-inflammatory drugs on the prevention of trans-operatory pain.

Regarding the absence of difference between the placebo and naproxen treatments after 24 hours, it is important to emphasize that the risk to tooth sensitivity was lower than expected (absolute risk ranging from 5% to 20%) regardless of the treatment. Furthermore, the risk to sensitivity reported during and immediately after the bleaching session was lower than the average observed in prior studies evaluating in-office bleaching procedures (0.63).[38] The same was observed for the level of sensitivity reported in the present study, while prior studies reported an average of 2.8 cm on the VAS.[38] The reduced sensitivity was probably due to the bleaching agent being more alkaline than those used in prior studies[2-4,20] and to the presence of calcium in the agent.[13] Furthermore, the elimination half-life (t½) of naproxen is achieved approximately 18 hours after its administration,[29] while slight effects of a single-dose use can be expected after 24 hours. This

Table 3: *Results (Medians and First and Third Quartiles) for Level of Tooth Sensitivity Observed for Each Treatment Using the Verbal Rating Scale*

Moment of Evaluation	First Session			Second Session			Average		
	Naproxen	Placebo	*p*-Value[a]	Naproxen	Placebo	*p*-Value[a]	Naproxen	Placebo	*p*-Value[b]
During	1.00 (0.00/2.00)	0.00 (0.00/1.00)	0.225	0.00 (0.00/1.00)	1.00 (0.00/1.00)	0.087	0.00 (0.00/1.00)	0.00 (0.00/1.00)	0.833
Immediately after	0.00 (0.00/0.00)	0.00 (0.00/1.00)	0.098	0.00 (0.00/0.00)	1.00 (0.00/1.00)	0.038	0.00 (0.00/1.00)	0.00 (0.00/1.00)	0.261
24 h after	0.00 (0.00/0.00)	0.00 (0.00/0.00)	0.162	0.00 (0.00/0.00)	0.00 (0.00/0.00)	0.162	0.00 (0.00/0.00)	0.00 (0.00/0.00)	1.000

[a] *Mann-Whitney rank sum test.*
[b] *Wilcoxon signed rank test.*

Table 4: *Results (Means [Standard Deviations]) for Level of Tooth Sensitivity Observed for Each Treatment Using the Visual Analog Scale*

Moment of Evaluation	First Session			Second Session			Average		
	Naproxen	Placebo	*p*-Value[a]	Naproxen	Placebo	*p*-Value[a]	Naproxen	Placebo	*p*-Value[b]
During	2.51 (2.09)	1.66 (2.05)	0.108	0.99 (1.01)	1.88 (1.85)	0.018	1.75 (2.11)	1.77 (1.94)	0.587
Immediately after	2.09 (2.19)	2.00 (2.25)	0.406	1.03 (1.54)	2.24 (2.31)	0.004	1.56 (1.95)	2.12 (2.26)	0.039

[a] *Mann-Whitney rank sum test.*
[b] *Wilcoxon signed rank test.*

t½ of naproxen also demonstrated that the one-week washout period used in this study, which is nine times higher than the t½, was enough to avoid any residual effect of the naproxen administered in the first session.

In addition to evaluating tooth sensitivity, color alteration reached with the bleaching procedures was also evaluated. Clinical trials evaluating bleaching procedures commonly expect at least 30 days for color to stabilize prior to final color measurement.[39] A shorter time was used in the present study because the main aim was to evaluate tooth sensitivity reported by patients instead of the effectiveness of the bleaching technique. Thus, the statistical analysis performed for color evaluation did not aim to compare the effect of treatment (naproxen or placebo) on bleaching effectiveness. Instead, the color evaluation aimed to determine whether bleaching procedures performed in patients allocated in both sequences of treatments resulted in tooth bleaching, demonstrating the action of hydrogen peroxide which is also responsible for tooth sensitivity. In fact, the bleaching procedure carried out in the present study resulted in a similar bleaching effect observed as prior studies using the same tool for color evaluation.[4,38,40,41] A recent meta-analysis analyzing data from clinical trials demonstrated an average of 5.3 (±2.8) ΔSGU when in-office tooth bleaching was carried out, which is slightly superior to the color alteration observed in the present study.[38]

Table 5: *Means (Standard Deviations) of ΔSGU[a]*

Sequence of Treatment	After First Session	After Second Session	Pooled Average
Placebo/naproxen	3.9 (1.0)	4.4 (0.9)	4.3 (1.3) a
Naproxen/placebo	3.7 (1.1)	4.9 (1.2)	4.1 (1.0) a
Pooled average	3.8 (1.0) A	4.7 (1.1) B	

Abbreviation: ΔSGU, change in the number of shade guide units.
[a] *For pooled average, different letters indicate significant statistical differences (α=0.05).*

An approximate 57% reduction of tooth sensitivity was observed only after the second session, when a reduction in the intensity level of sensitivity was also reported. This reduction on risk was slightly superior to that observed using a desensitizing gel containing nitrate potassium/sodium fluoride in previous studies (30% to 46%).[16,42] However, overall, administrating a single dose of naproxen prior to a bleaching procedure did not affect risk and level of tooth sensitivity. The crossover design of the present study aimed to reduce bias related to population (age, gender, and so on) in relation to tooth sensitivity. Despite this experimental design eliminating the difference between evaluated treatments, the population studied presented a predominance of young (median age of 23 years) and female patients (64%). Pain threshold differences between genders have been demonstrated, so the outcomes found in the present study could be different if more men were evaluated.[43] Furthermore, outcomes from young patients cannot generalize to a general population of older adults.[38,44] Further studies evaluating different populations or other anti-inflammatories, doses, or administration protocols are required to clarify the evidence about the preemptive administration of anti-inflammatories on tooth sensitivity caused by in-office bleaching.

CONCLUSION

The preemptive administration of naproxen in a single dose one hour prior to an in-office bleaching procedure has limited effect on the risk and level of tooth sensitivity reported by patients and a reduction in sensitivity was only observed immediately after a second session. Moreover, no alteration on bleaching effectiveness was observed by administration of naproxen.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the committee for the protection of human subjects of the Federal University of Sergipe. The approval code for this study is CAAE: 37578714.4.0000.5546.

Conflict of Interest

The authors of this article certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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