RESEARCH PAPER

# Comparative Efficacy of Topical 10% Pregabalin and 1% Ibuprofen Gels in Managing In-Office Bleaching-Induced Tooth Sensitivity

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## ABSTRACT

Objective: To compare the clinical efficacy of topical 10% pregabalin gel and 1% nanostructured ibuprofen gel in reducing tooth sensitivity following in-office bleaching with 35% hydrogen peroxide.

Methods: A randomized split-mouth clinical trial was conducted in 16 adult volunteers. After prophylaxis and gingival isolation, the assigned gel was applied to anterior teeth for 10 minutes before bleaching and reapplied for 10 minutes after bleaching. Sensitivity was assessed using a 10-cm Visual Analog Scale (VAS) at predefined follow-up intervals. Between-group comparisons used the Mann–Whitney U test; within-group changes used Friedman two-way ANOVA with post-hoc comparisons.

Results: Mean VAS scores were significantly lower with pregabalin than ibuprofen on Day 1 (1.5±0.527 vs 3.9±0.738), Day 2 (0.7±0.675 vs 2.5±0.527), and Days 3–7 (0.3±0.483 vs 2.1±0.568), all $p<0.001$. Differences persisted on Day 8 (1.5 vs 4.1; $p<0.001$), Day 9 (0.9 vs 2.1; $p=0.002$), and Days 10–14 (0.4 vs 1.4; $p=0.003$).

Conclusion: Within the study limitations, topical 10% pregabalin gel demonstrated greater reduction in bleaching-induced tooth sensitivity than 1% nanostructured ibuprofen gel.

Keywords: Tooth sensitivity; dental bleaching; in-office bleaching; pregabalin; ibuprofen; desensitizing agents; randomized clinical trial.

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## INTRODUCTION

Tooth bleaching is a conservative aesthetic procedure for localized or generalized discoloration which offers an effective approach to improving tooth colour while preserving the natural tooth structure[3]. The whitening effect is primarily achieved through the action of oxidizing agents, most commonly hydrogen peroxide (HP) and carbamide peroxide (CP)[4] .These generate reactive oxygen species that break down chromophores and lighten tooth colour.[1], [5], act on both extrinsic stains present on the tooth surface and intrinsic discolorations located within enamel and dentin [6]

In-office bleaching commonly uses 35–40% hydrogen peroxide and is frequently associated with transient tooth sensitivity. Hydrogen peroxide can diffuse through enamel and dentinal tubules, reach the pulp and induce oxidative stress, cellular injury and transient inflammatory responses.[7,8] .The penetration of peroxide into the pulp can induce oxidative stress, cellular damage and a reduction in the viability of dental pulp cells [9]Bleaching

sensitivity is clinically expressed through stimulation of pulpal nociceptive pathways. Inflammatory mediators and transient receptor potential channels, particularly TRPA1 and TRPV1, contribute to pain perception.[10],[11]

Systemic analgesics and anti-inflammatory drugs have not consistently prevented bleaching sensitivity, encouraging topical delivery approaches that place pharmacological agents closer to the site of pain generation.[2],[12]

Pregabalin binds the α2δ subunit of voltage-gated calcium channels, reducing calcium influx and neuronal excitability.[13],[14] Topical pregabalin therefore offers a potential localized neural-modulating approach. Ibuprofen inhibits cyclooxygenase and prostaglandin synthesis; nanostructured delivery may improve drug dispersion and tissue contact.[15],[16]

The present study aimed to compare experimental 10% pregabalin gel with 1% nanostructured ibuprofen gel for reducing tooth sensitivity following in-office bleaching with 35% hydrogen peroxide.

## MATERIALS AND METHODS

A randomized split-mouth clinical trial was conducted in 16 adult volunteers. An a priori G*Power calculation used a one-tailed test comparing two independent means, Cohen's d=1.3373332, α=0.05, power=80% and allocation ratio 1:1. The calculated sample was eight participants per group (16 total), with actual power 0.81519.

The protocol was approved by the Institutional Ethics Committee of Panineeya Mahavidyalaya Institute of Dental Sciences & Research Centre, Hyderabad (IEC No. PMVIDS&RC/IEC/CONS/PR/651-25). Sixteen volunteers of both sexes, aged 18–35 years, with good general and oral health, at least 28 teeth, and mandibular canines of shade A2 or darker were included. Teeth were caries-free, unrestored and free from periodontal disease, and participants had no previous bleaching. Participants with prostheses/orthodontic appliances, severe tetracycline/fluorosis/trauma/necrosis-related discoloration, pregnancy/lactation, smoking, bruxism, gingival recession, dentinal exposure, extensive cracks, continuous analgesic/anti-inflammatory medication or ibuprofen allergy were excluded.

The 10% pregabalin gel was prepared by incorporating pregabalin solution (10 mg/mL) into 1% Carbopol 940 gel containing methylparaben, propylparaben, EDTA, propylene glycol, 50% triethanolamine and distilled water.[22] The 1% nanostructured ibuprofen gel contained ibuprofen 1%, soybean oil 1%, soybean phosphatidylcholine 0.75%, polysorbate 80 0.25%, co-solvent 10%, poloxamer 407 15% and water 72%.[23]

Prophylaxis was performed using a rubber cup and pumice, followed by a protective gingival barrier. According to randomization, pregabalin or ibuprofen gel was applied with a microbrush to the buccal surfaces of the central incisors, lateral incisors and canines for 10 minutes before bleaching. In-office bleaching was performed with 35% hydrogen peroxide, followed by reapplication of the respective gel for 10 minutes. The gels and bleaching material were then removed and the area rinsed.

Sensitivity was assessed using a 10-cm VAS, with 0 representing no sensitivity and 10 severe sensitivity. Participants recorded sensitivity in a diary at predefined intervals including immediately after treatment, 1 hour, 24 hours, 48 hours, Days 3–7 and subsequent follow-up periods. The highest VAS score during each specified assessment period was used for intensity analysis.

Data were analyzed using non-parametric tests. The Mann–Whitney U test compared VAS scores between groups. Within-group changes were evaluated using Friedman two-way ANOVA followed by post-hoc pairwise comparisons where appropriate. A p-value ≤0.05 was considered statistically significant.

## RESULTS

The mean VAS scores were lower in the pregabalin group than in the ibuprofen group during both weeks. During the first week, significant between-group differences were observed on Day 1, Day 2 and Days 3rd–7th (all p<0.001). During the second week, significant differences were observed on Day 8 (p<0.001), Day 9 (p=0.002), and Days 10th–14th (p=0.003). Within-group Friedman Two-Way ANOVA was significant for the pregabalin group (test statistic 26.259; p<0.001) and the ibuprofen group (test statistic 39.610; p<0.001). The complete descriptive and inferential results are presented in Tables 1–4, with post-hoc pairwise comparisons in Tables 3a and 4a.

Table 1: Mean comparison of VAS scores between the groups in the 1st week

| Timeline | Groups | n | Mean | SD | Median | Interquartile range | Test statistic value | P value |
|---|---|---|---|---|---|---|---|---|
| Da | Pre | 8 | 1. | 0.5 | 1.5 | 1.00 | - | **<0.** |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| y 1 | gabalin | | 5000 | 2705 | 000 | 00-2.000 | 3.876 | **001*** |
| | Ibuprofen | 8 | 3.9000 | 0.73786 | 4.0000 | 3.0000-4.250 | | |
| Day 2 | Pregabalin | 8 | 0.7000 | 0.67495 | 1.0000 | 0.0000-1.000 | -3.711 | **<0.001*** |
| | Ibuprofen | 8 | 2.5000 | 0.52705 | 2.5000 | 2.0000-3.000 | | |
| Day 3rd-7th | Pregabalin | 8 | 0.3000 | 0.48305 | .0000 | 0.0000-1.000 | -3.849 | **<0.001*** |
| | Ibuprofen | 8 | 2.1000 | 0.56765 | 2.0000 | 2.0000-2.250 | | |

Table 2: Mean comparison of VAS scores between the groups in the 2nd week

| Timeline | Groups | n | Mean | SD | Median | Interquartile range | Test statistic val | Pvalue |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | ue | |
| Day 8 | Pregabalin | 8 | 1.5000 | 0.52705 | 1.5000 | 1.0000-2.000 | -3.876 | **<0.001*** |
| | Ibuprofen | 8 | 4.1000 | 0.73786 | 4.0000 | 3.7500-5.000 | | |
| Day 9 | Pregabalin | 8 | 0.9000 | 0.73786 | 1.0000 | 0.0000-1.250 | -3.103 | **0.002*** |
| | Ibuprofen | 8 | 2.1000 | 0.56765 | 2.0000 | 2.0000-2.250 | | |
| Day 10th-14th | Pregabalin | 8 | 0.4000 | 0.51640 | 0.0000 | 0.0000-1.000 | -3.130 | **0.003*** |
| | Ibuprofen | 8 | 1.4000 | 0.51640 | 1.0000 | 1.0000-2.000 | | |

Table 3: Mean comparison of VAS scores within the Pregabalin group

| Timeline | n | Mean | SD | Median | IQR | Test statistic valu | Pvalue |
|---|---|---|---|---|---|---|---|

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | e | |
| Day 1 | 8 | 1.5000 | 0.52705 | 1.5000 | 1.0000-2.000 | 26.259 | **<0.001*** |
| Day 2 | 8 | 0.7000 | 0.67495 | 1.0000 | 0.0000-1.000 | | |
| Day 3rd – 7th | 8 | 0.3000 | 0.48305 | 0.0000 | 0.0000-1.000 | | |
| Day 8 | 8 | 1.5000 | 0.52705 | 1.5000 | 1.0000-2.000 | | |
| Day 9 | 8 | 0.9000 | 0.73786 | 1.0000 | 0.0000-1.250 | | |
| Day 10th – 14th | 8 | 0.4000 | 0.51640 | 0.0000 | 0.0000-1.000 | | |

Table 3a: Pairwise comparison – post hoc analysis

| Comparison between | | P value |
|---|---|---|
| Day 1 | Day 2 | 0.405 |
| | Day 3rd – 7th | **0.008*** |
| | Day 8 | 0.905 |
| | Day 9 | 0.837 |
| | Day 10th – 14th | **0.002*** |
| Day 2 | Day 3rd – 7th | 0.209 |
| | Day 8 | 0.547 |
| | Day 9 | 0.765 |
| | Day 10th – 14th | 0.403 |
| Day 3rd – 7th | Day 8 | **0.012*** |
| | Day 9 | 0.120 |
| | Day 10th – 14th | 0.676 |
| Day 8 | Day 9 | 0.073 |
| | Day 10th – 14th | **0.003*** |
| Day 9 | Day 10th – 14th | 0.256 |

Table 4: Mean comparison of VAS scores within the Ibuprofen group

Table 4a: Pairwise comparison – post hoc analysis

**DISCUSSION**

Bleaching-induced tooth sensitivity is one of the most frequently encountered adverse effects associated with in-office tooth whitening. Although bleaching provides an effective and conservative method of improving tooth colour, sensitivity may negatively influence patient comfort, treatment acceptance and willingness to undergo subsequent procedures. Therefore, prevention and management of bleaching sensitivity remain important clinical considerations.

In the present study, 16 volunteers within the specified age range were included. Age is relevant to bleaching sensitivity because peroxide penetration toward the pulp is influenced by the structural characteristics and permeability of dental tissues. Younger teeth generally have a relatively larger pulp chamber and greater dentinal permeability [1], whereas secondary dentin deposition and tubular changes with age may reduce permeability [23]. The controlled age range helped limit variation attributable to age-related differences in dentinal permeability [1].

The biological mechanism of bleaching sensitivity is generally associated with transient pulpal inflammation and stimulation of sensory pathways. Hydrogen peroxide can diffuse through enamel and dentin and reach the pulp, where oxidative stress and cellular damage may occur [17]. The biological response involves inflammatory mediators (substance P, interleukin-1β, interleukin-6 and tumour necrosis factor-alpha) and stimulation of peripheral nociceptors [18]. Hydrogen peroxide has

also been reported to activate TRPA1 and TRPV1, which participate in dental pain transmission[19] .These mechanisms indicate that bleaching sensitivity is not exclusively an inflammatory phenomenon but involves inflammatory and neural components.

Systemic analgesics and anti-inflammatory drugs have shown inconsistent effectiveness for preventing bleaching sensitivity [2,12] .Systemically administered drugs undergo absorption, distribution, metabolism and excretion, while the tooth's rigid mineralized tissues and limited pulpal vascular supply may restrict drug availability at the site of peroxide-induced irritation. This provides a rationale for topical approaches ( local drug delivery)[16] in which the active agent is applied directly to the tooth surface.

Pregabalin was selected because its pharmacological action is directed toward neuronal excitability. Pregabalin binds with high affinity to the α2δ subunit of voltage-gated calcium channels and reduces calcium influx into nerve terminals[13,14]. Reduced calcium-dependent neurotransmitter release can decrease neuronal excitability and pain transmission. In the present study, 10% pregabalin gel was intended to provide localized pharmacological modulation of the sensory component of bleaching pain.

The principal finding was that 10% pregabalin gel produced consistently lower VAS scores than 1% nanostructured ibuprofen gel throughout follow-up. During the first week, the difference was marked on Day 1 and remained significant on Days 2 and 3–7. The difference persisted during the second week. The progressive reduction in VAS scores within the pregabalin group indicates lower sensitivity during observation, while the between-group results demonstrate a greater magnitude of reduction than with ibuprofen.

The effectiveness observed with pregabalin may be related to its action on neural mechanisms involved in pain transmission. Hydrogen peroxide-induced activation of TRPA1 and TRPV1 has been implicated in bleaching-related hyperalgesia[19]. Pregabalin does not directly function as an anti-inflammatory NSAID; rather, its modulation of voltage-gated calcium channels provides a mechanism for reducing neuronal excitability. It has also been suggested that pregabalin can influence downstream pathways associated with TRPV1 and NF-κB activation[13]. Thus, its potential benefit may involve modulation of neural signaling in addition to indirect effects on inflammatory pain pathways.

The present findings are consistent with the clinical investigation by Xavier et al. (2025), in which an experimental pregabalin gel was evaluated after bleaching with 35% hydrogen peroxide[14] .Their findings similarly supported the potential effectiveness of topical pregabalin in reducing bleaching-related sensitivity. Agreement between the clinical findings is relevant because both investigate topical pregabalin in the context of high-concentration in-office bleaching rather than systemic administration.

In contrast, the 1% ibuprofen nanostructured gel did not demonstrate comparable effectiveness. Ibuprofen is a well-established NSAID whose principal pharmacological action involves cyclooxygenase inhibition and reduction of prostaglandin synthesis[15]. Although suppression of inflammation can reduce pain, bleaching sensitivity is generated by a combination of inflammatory and neural mechanisms. Consequently, an agent acting primarily through prostaglandin inhibition may not adequately suppress the entire sensory response to peroxide penetration.

The concentration of ibuprofen may also have contributed to the observed difference. Hortkoff et al. (2024) evaluated a topical formulation containing 5% ibuprofen combined with 10% arginine and reported a reduction in the risk and intensity of bleaching sensitivity [21] . The present study used 1% ibuprofen without arginine. Therefore, the lower concentration may have resulted in lower drug availability at the target site, while the absence of arginine removed an additional desensitizing mechanism. The comparison should be interpreted as a comparison between the specific formulations tested rather than evidence that ibuprofen as a drug class is ineffective.

Another possible explanation for the lower effectiveness of ibuprofen is its limited relationship with neural mechanisms implicated in peroxide-induced hypersensitivity. In silico work has suggested relatively low binding affinity of ibuprofen for TRPA1, a receptor involved in peroxide-induced hyperalgesia[20]. Therefore, inhibition of prostaglandin production may suppress only one component of the pain pathway. In contrast, pregabalin's effect on voltage-gated calcium channels provides a mechanism for altering neuronal signaling.

Within these limitations, the present randomized split-mouth clinical trial suggests that topical 10% pregabalin gel may provide greater reduction in bleaching-induced tooth sensitivity than the tested 1% nanostructured ibuprofen gel. The result supports further investigation of topical neural-modulating agents as localized drug-delivery strategies for management of dental sensitivity.

## CONCLUSION

Within the limitations of the present study, 10% pregabalin gel was effective in reducing bleaching-induced tooth sensitivity following in-office bleaching with 35% hydrogen peroxide. The pregabalin group demonstrated significantly lower VAS scores than the 1% ibuprofen group throughout follow-up. The greater effectiveness of pregabalin may be related to modulation of neuronal calcium-channel activity and pain

transmission. Further clinical studies should evaluate optimized topical concentrations, larger samples, longer follow-up and molecular pathways involved in bleaching-induced pain.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

**REFERENCES**

1. Krishnakumar K, Tandale A, Mehta V, Khade S, Talreja T, Aidasani G, et al. Post-operative sensitivity and color change due to in-office bleaching with the prior use of different desensitizing agents: a systematic review. Cureus. 2022;14(4):1-8.

2. Silva KLD, Sutil E, Hortkoff D, Terra RMO, Rezende M, Reis A, et al. Coadministration of ibuprofen/caffeine on bleaching-induced tooth sensitivity: a randomized clinical trial. Braz Dent J. 2021;32(2):105-15.

3. Raut AW, Mantri V, Gedam PV, Phabyani PP. Conservative esthetic management of severe dental fluorosis with in-office power bleaching. Ann Afr Med. 2020;19(3):211-14.

4. De Moor RJG, Verheyen J, Diachuk A, Verheyen P, Meire MA, De Coster PJ, et al. Insight in the chemistry of laser-activated dental bleaching. Sci.World J.2015;2015(1):1-6.

5. Cavalli V, Kury M, Melo PBG, Carneiro RVTSM, Esteban Florez FL. Current status and future perspectives of in-office tooth bleaching. Front Dent Med. 2022;3:1-10.

6. Féliz-Matos L, Hernández LM, Abreu N. Dental bleaching techniques: hydrogen-carbamide peroxides and light sources for activation, an update. Open Dent J. 2015;8(1):264-68.

7. Mena-Serrano AP, Parreiras SO, Nascimento EMS, Borges CPF, Berger SB, Loguercio AD, et al. Effects of the concentration and composition of in-office bleaching gels on hydrogen peroxide penetration into the pulp chamber. Oper Dent. 2015;40(2):76-82.

8. Alqahtani MQ. Tooth-bleaching procedures and their controversial effects: a literature review. Saudi Dent J. 2014;26(2):33-46.

9. Donato MV, Dos Reis-Prado AH, Abreu LG, de Arantes LC, Goto J, Chaves HGDS, et al. Influence of dental bleaching on the pulp tissue: a systematic review of in vivo studies. Int Endod J. 2024;57(6):630-54.

10. Silva-Costa RSGD, Ribeiro AEL, Assunção IV, Araújo Júnior RF, Araújo AA, Guerra GCB, et al. In-office tooth bleaching with 38% hydrogen peroxide promotes moderate/severe pulp inflammation and production of IL-1β, TNF-β, GPX, FGF-2 and osteocalcin in rats. J Appl Oral Sci. 2018;26(0):1-9.

11. Chen C, Huang X, Zhu W, et al. TRPA1 triggers hyperalgesia and inflammation after tooth bleaching. Sci Rep. 2021;11(1):1-12.

12. Carregosa Santana M, Leal P, Reis A , Silva A.Effect of anti-inflammatory and analgesic drugs for the prevention of bleaching-induced tooth sensitivity.J Am Dent Assoc.2019; 150 (10):818-29.

13. Alles SRA, Cain SM, Snutch TP. Pregabalin as a pain therapeutic: beyond calcium channels. Front Cell Neurosci. 2020;14(0):1-9.

14. Xavier GMB, Paes YFO, de Meneses Costa Ferreira LM, Lamarão MLN, Silva CM, Ribeiro-Costa RM, et al. Effect of an experimental pregabalin gel on dental sensitivity and color change after bleaching with 35% hydrogen peroxide: a randomized clinical trial. Clin Oral Investig. 2025;29(3):1-10.

15. de Oliveira FJD, de Sá Barbosa BF, de Bessa MS, et al. Efficacy of a 1% ibuprofen nanostructured topical gel in reducing in-office bleaching sensitivity following 35% hydrogen peroxide application: a randomized, controlled, triple-blind, split-mouth clinical trial. Clin Oral Investig. 2025;29(6):1-9.

16. Shahri F, Parhizkar A. Pivotal local drug delivery systems in endodontics: a review of literature. Iran Endod J. 2020;15(2):65-78.

17. Cintra LTA, Benetti F, Ferreira LL, Gomes-Filho JE, Ervolino E, Gallinari MO, et al. Penetration capacity, color alteration and biological response of two in-office bleaching protocols. Braz Dent J. 2016;27(2):169-75.

18. Soares DG, Sacono NT, Ribeiro APD, Leite ML, Duque CCO, Gallinari MO, et al. Pro-inflammatory mediators expression by pulp cells following tooth whitening on restored enamel surface. Braz Dent J. 2022;33(1):83-90.

19. Hossain MZ, Mohd Bakri M, Yahya F, et al. The role of transient receptor potential (TRP) channels in the transduction of dental pain. Int J Mol Sci. 2019;20(3):1-31.

20. Irvine J, Afrose A, Islam N. Formulation and delivery strategies of ibuprofen: challenges and opportunities. Drug Dev Ind Pharm. 2018;44(2):173-83.

21. Hortkoff D, da Silva KL, Farago PV, Gomes JC, Reis A, Gomes GM. Effect of topical application of ibuprofen/arginine on the in-office bleaching-induced tooth sensitivity: a randomized, triple-blind controlled trial. J Dent. 2024;142(0):1-8.

22. Xavier GMB, Ferreira LM, de Passos MCMF, et al. Characterization and evaluation of the cytotoxicity of pregabalin gels for oral application. Pharmaceuticals (Basel). 2024;17(9):1-14.

23. de Oliveira Gallinari M, Ângelo Cintra LT, Benetti F, et al. Pulp response of rats submitted to bleaching and the use of different anti-inflammatory drugs. PLoS One. 2019;14(1):1-14.