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Review
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Strategies to enhance local anesthesia efficacy in molar-incisor hypomineralization affected teeth: A systematic review

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Highlights

- Teeth affected by molar-incisor hypomineralization show increased dentin–pulp sensitivity and pulpal inflammation, which reduces the predictability of local anesthesia.
- The use of 4% articaine, preemptive analgesia, intraosseous anesthesia, and cryotherapy has been proposed to improve anesthetic efficacy in MIH-affected teeth.
- Current findings are based on small, heterogeneous studies; larger, standardized trials are needed for definitive recommendations.

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Abstract

Molar-incisor hypomineralization increases dentin–pulp sensitivity and is frequently associated with chronic pulpal inflammation, which may reduce the effectiveness of conventional local anesthesia. This systematic review aimed to evaluate clinical strategies to improve local anesthesia efficacy in teeth affected by molar-incisor hypomineralization and to provide evidence-based recommendations for clinical practice. A PRISMA-guided literature search was conducted in PubMed/MEDLINE, Web of Science, Scopus, and ScienceDirect using terms related to "molar-incisor hypomineralization" and "anesthesia." Studies evaluating interventions designed to enhance anesthetic efficacy in MIH-affected teeth were included, while reviews, case reports, in vitro studies, and studies conducted outside an MIH context were excluded. Data were synthesized qualitatively. Seven eligible clinical studies were identified. Articaine 4% demonstrated superior anesthetic efficacy compared with lidocaine, particularly in mandibular molars. Intraosseous anesthesia showed high success rates and rapid onset in difficult-to-anesthetize cases. Preemptive administration of ibuprofen was associated with reduced pulpal inflammation and improved anesthetic effectiveness. Cryotherapy applied following nerve block reduced intraoperative pain, especially in anxious patients. Photobiomodulation did not demonstrate a significant benefit in enhancing anesthetic efficacy. The main limitations of the included studies were small sample sizes, heterogeneity in study designs, and reliance on subjective pain assessments, with no large-scale randomized controlled trials available. Current evidence supports the use of articaine 4% as the preferred local anesthetic agent, the administration of preemptive analgesia, the consideration of intraosseous anesthesia for challenging mandibular MIH cases, and the adjunctive use of cryotherapy following nerve block. Photobiomodulation cannot be recommended at present. Future research should prioritize well-designed, adequately powered randomized clinical trials to confirm these findings and establish standardized clinical protocols.

Keywords: Analgesia; Local Anesthesia; Pain; Tooth Hypomineralization; Treatment Outcome

INTRODUCTION

Molar-incisor hypomineralization is a developmental enamel defect of systemic-origin that affects one to four permanent first molars, and it is often associated with involvement of permanent incisors.[1] Clinically, it is characterized by well-demarcated white, yellow or brown opacities, with affected enamel exhibiting varying degrees of porosity and hypomineralization.[1-4] Due to its structural weakness, this enamel is prone to post-eruptive breakdown, particularly on the occlusal surfaces.[1, 4] This condition is recognized globally as an important public health problem, with prevalence estimations ranging widely. Reported prevalence rates for MIH vary widely, ranging from approximately 4% to 36%.[4] Although no single etiological factor has been identified, systemic conditions occurring during the first three years of life, such as upper respiratory tract infections, asthma, and viral childhood illnesses, have been associated with its development.[2]

Managing dental care in children with MIH is particularly difficult because these children are highly sensitive to stimuli such as air, cold, warmth, and brushing, which often causes considerable discomfort during oral hygiene. Depending on the degree of hypersensitivity, difficulties with toothbrushing, a higher risk of poor oral hygiene, and eating problems which can impact the child's diet and growth, may arise, further complicating prevention and treatment. Hypersensitivity is especially pronounced in MIH-affected teeth with enamel breakdown or atypical restorations.[5-7] Moreover, several studies indicate that children with MIH have a higher risk of developing caries than those without MIH,[8-10] as well as aesthetic defects associated with MIH.[1, 11] Collectively, these factors adversely affect the oral health–related quality of life (OHRQoL) of both children and their parents.[12-14] A systematic review reported that children with MIH experience significantly lower OHRQoL, about 17–25 times worse, than unaffected peers.[15] Even after restoration of teeth with substantial structural loss, hypersensitivity often does not disappear completely but diminishes, resulting in an overall improvement in quality of life.[16]

The heightened sensitivity in MIH-affected teeth is multifactorial. Increased enamel porosity enhances permeability, allowing thermal, chemical, and mechanical stimuli to directly affect the underlying dentin and pulp.[3, 17] In addition, the rapid progression of caries in these compromised teeth frequently results in chronic pulpal inflammation, even in the absence of overt symptoms.[18] This subclinical or chronic inflammation triggers a cascade of neurophysiological changes within the pulp, including a lowered excitability threshold of nerve fibers, elevated levels of inflammatory mediators, and structural alterations in nerve morphology. In addition to local inflammatory changes, salivary proteomic profiles in MIH-prone individuals often reveal shifts toward a catabolic protein environment, indicating ongoing tissue turnover and degradation as well as the presence of mediators that may sensitize nociceptors or promote neurogenic inflammation.[19] Collectively, these mechanism contribute to hyperalgesia and render the pulp less responsive to the effects of local anesthetic agents.[2, 20] As a result, conventional anesthetic techniques that are typically effective in healthy teeth often fail to provide adequate pain control in MIH cases, leading to painful treatment experiences, increased anxiety, and significant behavioral management challenges for the dentist.[3, 21]

Recent proteomic analyses of saliva and gingival crevicular fluid (GCF) in MIH patients converge on a common inflammatory, proteolytic, and altered mineralization profile that may underlie anesthesia challenges.[19, 22-24] Saliva from MIH individuals shows a distinct proteome with 88 unique proteins, enriched for neutrophil degranulation and neutrophil-mediated immunity,

and elevated inflammatory markers such as complement C5, plasma kallikrein, IL-18, IL36RN, and CCL28, along with tissue-degrading enzymes like PREP and CAPN2, collectively indicating a chronic inflammatory and catabolic milieu. [19] Severity-linked changes include shifts in molecular functions related to calcium binding and cytoskeletal proteins, suggesting a link between the extent of structural defect and pain processing. GCF analyses corroborate local inflammation, revealing higher periodontal indices and increased GCF volume in MIH-affected sites. Importantly, MMP-20 has emerged as a promising diagnostic biomarker, being reduced in MIH and demonstrating high sensitivity and specificity for MIH status. [22] Collectively, these findings support a model in which saliva and GCF biomarkers reflect an inflammatory, proteolytic environment with altered mineralization that may influence anesthetic efficacy in MIH, highlighting potential pathways for diagnosis and analgesic guidance.

Failure to achieve profound anesthesia not only compromises the quality of dental treatment but also reinforces a cycle of dental fear and avoidance in young patients. Therefore, identifying and applying effective strategies to enhance local anesthesia in MIH-affected teeth is essential for ensuring successful clinical outcomes, improving patient comfort, and fostering positive dental experiences. A systematic assessment of current evidence is essential to establish a robust, universally applicable clinical protocol for MIH management, one that enhances patient comfort, improves behavioral outcomes, and increases the clinical success of restorative and endodontic procedures in this challenging pediatric population. Accordingly, this systematic review aims to synthesize the available evidence on methods used to address anesthetic challenges in MIH, providing a comprehensive overview of their efficacy and offering evidence-based recommendations for clinical practice.

METHODS

In this review, the PRISMA[25] criteria were followed, and the literature search was structured. The aim was to identify publications addressing strategies to enhance efficacy of local anesthesia in MIH affected teeth. Electronic databases including PubMed/MEDLINE, Sciencedirect, and Web of Science were searched using the following keywords and MeSH terms: *"molar incisor hypomineralization"* AND (*"anesthesia"* OR *"anaesthesia"*) (Figure 1). The search was conducted on August 11, 2025

Inclusion criteria comprised studies evaluating different methods or agents aimed at improving local anesthesia in patients diagnosed with MIH. Exclusion criteria included review articles, case reports, in vitro studies, and studies not directly related to local anesthesia in MIH. Search results were exported to RStudio, duplicates were removed, and remaining records were organized in an Excel file. Two independent researchers screened titles, abstracts, and full texts to identify eligible studies. Each reviewer independently selected articles for inclusion, and their selections were compared for concordance. Any disagreements were resolved through further in-text review and discussion until consensus was reached. For each study, data were extracted on: study design, sample size, MIH severity, intervention type (anesthetic agent, technique, or adjunctive therapy), outcome measures (e.g., pain perception, anesthetic success rate, need for supplemental anesthesia), and main findings. The subcategories were defined to (a) differentiate evidence by methodological quality and design, (b) contextualize the precision and generalizability of results through sample size, (c) enable meaningful comparisons across different anesthesia strategies (agents, techniques, adjuncts), (d) focus on clinically relevant endpoints directly related to anesthesia efficacy, and (e) summarize findings to identify promising approaches and evidence gap.

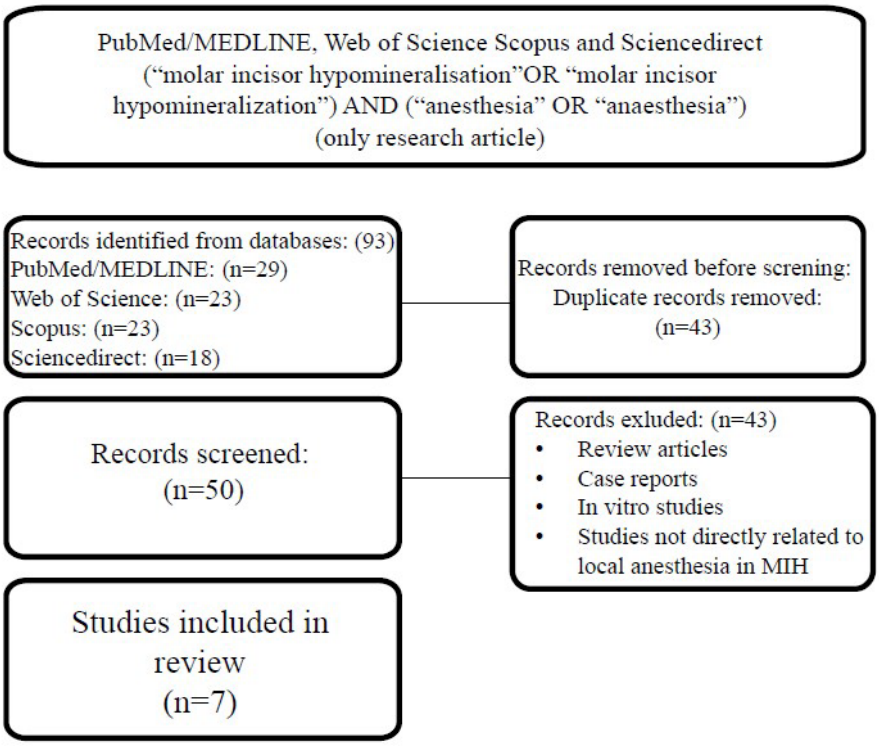

Figure 1. Flow diagram of the study search process

Cochrane RoB-2 tool for randomized controlled trials (RCTs) and ROBINS-I tool for non-randomized interventional studies were used to assess risk of bias[26]. RoB-2 tool evaluates five domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of the reported results, with judgments categorized as low, some concerns, or high risk of bias. ROBINS-I assesses seven domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, outcome measurement, and selection of reported results, with an overall risk of bias rating ranging from low to critical. Two independent reviewers performed the assessments, resolving any disagreements by discussion and consensus.

RESULTS

A total of seven articles met the inclusion criteria for this systematic review, each exploring various strategies to improve local anesthesia effectiveness in MIH affected teeth (Table 1).

The interventions examined in these studies can be grouped into three main thematic categories:

1. Anesthetic agent selection: comparing the clinical performance of different local anesthetics in MIH-affected teeth.
2. Advanced anesthetic techniques: evaluating alternative delivery approaches, such as intraosseous anesthesia.
3. Adjunctive therapies: assessing the role of pharmacological and non-pharmacological measures (e.g., preemptive analgesia, cryotherapy, photobiomodulation) in improving anesthetic outcomes.

Table 2 presents assessment of all studies based on the appropriate risk of bias tool (Cochrane RoB-2 for RCTs and ROBINS-I for non-randomized interventional studies).

Table 1. Summary of included studies on strategies to enhance local anesthesia efficacy in MIH affected teeth

Study (Year)	Study Design	Sample Size	MIH severity in teeth	Intervention(s)	Outcome Measures	Key Findings	Limitations/ Notes
Thomas et al. (2023)[27]	RCT	27 cases (8-12 years)	Spontaneous pain and irreversible pulpitis in molars affected by MIH	4% articaine buccal infiltration (BI) 4% articaine IANB, 2% lignocaine IANB	Pain perception (VAS) during root canal treatment (access opening, instrumentation)	4% articaine IANB showed better anesthetic efficacy than 4% articaine BI and 2% lignocaine IANB.	Small sample size.
Haidar & Raslan (2023)[28]	RCT (Crossover)	20 cases (40 teeth) (6-12 years)	Affected by MIH with a score of 2, 3 or 5 according to Ghanim's index[29]	4% articaine IANB vs. 2% lidocaine IANB	Injection pain (Wong-Baker, FLACC), effectiveness of Anesthesia (Wong-Baker, FLACC), complications	Articaine injection caused more pain on administration. Both agents were effective, but articaine was clinically more effective.	Small sample size.
Dixit & Joshi (2018)[30]	RCT	29 cases (54 teeth) (8-14 years)	Evaluated by modified Wetzel and Reckel scale[31]	Intraosseous (IO) anesthesia (X-tip system) with 4% articaine vs. conventional local infiltration (4% articaine)	Onset time, pain during administration, need for repeat injection, efficacy, heart rate, postoperative complications	IO anesthesia is significantly more effective (88.9% profound anesthesia) than infiltration (74.1% failure). Faster onset, less pain during administration, fewer complications.	Split-mouth design assessing maxillary and mandibular teeth separately suggested.
Vicioni-Marques et al. (2022)[32]	Triple-blind RCT	23 cases (23 teeth) (6-10 years)	MIH-affected molars with post-eruptive enamel breakdown, and hypersensitivity.	Preemptive ibuprofen (10 mg/kg) vs. placebo	Hypersensitivity (Wong-Baker scale) at multiple time points (before/after drug, before/after anesthesia, during and 2h post procedure)	Preemptive ibuprofen significantly increased anesthetic efficacy and improved comfort by reducing hypersensitivity	Broad age range, subjective pain assessment

Table 1. Summary of included studies on strategies to enhance local anesthesia efficacy in MIH affected teeth (continued)

Study (Year)	Study Design	Sample Size	MIH severity in teeth	Intervention(s)	Outcome Measures	Key Findings	Limitations/ Notes
Contac et al (2024)[33]	Clinical Study	27 cases (27 teeth) (5-7 years)	MIH treatment need index (TNI) score of 4 [11]and level 3 posteruptive breakdown.	Preemptive ibuprofen + standardized anesthesia + behavioral strategies	Pain intensity (Wong-Baker, FLACC) at 6 time points	Preemptive analgesia significantly improved intraoperative pain control and behavioral outcomes.	No control group for direct comparison of preemptive analgesia alone.
Peedikayil et al. (2024)[34]	RCT (Split-mouth)	28 cases (56 teeth) (8-12 years)	MIH TNI criteria 4[11] (MIH with breakdown)	IANB + cryotherapy vs. IANB alone	Intraoperative pain (VAS, FLACC)	Cryotherapy significantly reduced intraoperative pain and sensitivity when combined with IANB.	Limited to mandibular molars
Aykanat & Elbay (2024)[35]	RCT (Triple-blind, Parallel-arm)	70 cases (70 teeth) (7-12 years)	Severe MIH according to the EAPD criteria[6]	Photobiomodulation therapy (PBMT) + infiltration anesthesia vs. placebo + infiltration anesthesia	Pain scores (FLACC) need for supplemental anesthesia	No significant difference in pain scores or supplemental anesthesia requirement between groups.	Limited to maxillary molars requiring pulpotomy.

IANB; Inferior Alveolar Nerve Block, BI; Buccal Infiltration, VAS; Visual Analogue Scale, FLACC; Face, Legs, Activity, Cry, Consolability pain assessment scale, IO; Intraosseous anesthesia, PBMT; Photobiomodulation Therapy, RCT: Randomized Clinical Trial

DISCUSSION

This review of seven studies provides valuable insights into strategies for improving the efficacy of local anesthesia in teeth affected by MIH. Across the literature, a consistent finding is that conventional anesthetic techniques often fail in MIH cases, necessitating alternative agents, delivery methods, or adjunctive therapies to achieve profound pain control.

Comparisons between articaine and lidocaine consistently indicate that articaine offers superior performance in MIH-affected teeth.[27, 28] The advantage is linked to its unique chemical structure, which includes a thiophene ring instead of a benzene ring, increasing its lipid solubility. This lipid solubility enhances diffusion through both soft and hard tissues. The result is a faster onset and more profound anesthesia, even in inflamed tissues.[36] Inflammation in MIH-affected pulp presents a lower pH, thereby lowering the proportion of non-ionized anesthetic molecules capable of penetrating nerve membranes.

Table 2. Comprehensive risk of bias assessment for evidence on anesthesia efficacy in MIH

Study (Year) / Tool Used	Comparison / Design Type	Key Risk Domain Assessment*	Major Concerns / Justification	Overall Risk of Bias
Haidar & Raslan (2023)[28] *(RoB-2)*	4% Articaine IANB vs. 2% Lidocaine IANB (Cross-over RCT)	D1, D2, D4: Low Risk	Study employed triple-blinding (child/parent, investigator, assessors), ensuring effective control of performance and detection bias.	**Low Risk**
Thomas et al. (2023)[27] *(RoB-2)*	4% Articaine BI vs. 4% Articaine IANB vs. 2% Lignocaine IANB (Parallel RCT)	D2, D4: Some concerns	Small sample size (n=9 per group) limits precision. Blinding status (operator/assessor) of operator not specified, raising concerns for performance bias.	**Some Concerns**
Vicioni-Marques et al. (2022)[32] *(RoB-2)*	Ibuprofen (10 mg/kg) vs. Placebo (Triple-blind RCT)	D1, D2, D4: Low Risk	Rigorous triple-blind design. Minor concern about sample size estimation.	**Low Risk**
Dixit & Joshi (2018)[30] *(RoB-2)*	Intraosseous (IO) Anesthesia vs. Buccal Infiltration (BI) (Both 4% Articaine) (Parallel RCT)	D2: High Risk	Intraosseous technique (X-tip system) inherently visible and operator-dependent. Operator and patient blinding are impossible, leading to a high risk of performance bias.	**High Risk**
Peedikayil et al. (2024)[34] *(RoB-2)*	IANB alone vs. IANB + Cryotherapy (Split-mouth RCT)	D2: Some Concerns	Study was double-blind (patient/observer). However, operator applied cryotherapy, making operator blinding impossible and introducing potential performance bias.	**Some Concerns**
Aykanat & Elbay (2024)[35] *(RoB-2)*	Photobiomodulation (PBMT) + Infiltration vs. Placebo + Infiltration (Triple-blind RCT)	D1, D2, D4: Low Risk	Excellent methodology, achieved triple-blinding with separate laser practitioner (unblinded) and an injection operator (blinded).	**Low Risk**
Contac et al. (2024)[33] *(ROBINS-I)*	Ibuprofen (Pre-post comparison: T1 [Failed] vs. T4 [Ibuprofen + Success]) (Non-randomized)	D1 Moderate D4: Serious Risk	Lack of blinding: Clinicians and patients were aware of ibuprofen use after the initial anesthetic failure (T1), introducing severe performance/expectation bias. Sequential design is confounded by behavioral strategies.	**Serious Risk**

*D1 = Randomization process; D2 = Deviations from intended interventions; D3 = Missing outcome data; D4 = Measurement of the outcome; D5 = Selection of the reported result. Risk of bias was judged as Low, Some concerns, or High according to the Cochrane RoB-2 tool for randomized trials, and as Low, Moderate, Serious, or Critical according to the ROBINS-I tool for non-randomized studies.

Articaine's slightly lower pKa (7.8) compared to lidocaine (7.9) means that a greater proportion of the local anesthetic remains in its non-ionized form at physiological pH, improving its efficacy in acidic environments.[37] However, Haidar and Raslan[28] reported greater injection discomfort with articaine, potentially due to its higher concentration (4%) and vasoconstrictor content. Clinicians should weigh this transient discomfort against the potential for improved anesthetic success.

Intraosseous (IO) anesthesia demonstrated particularly promising results.[30] IO techniques provide rapid diffusion to the periapical nerve plexus by bypassing the dense cortical bone and delivering the anesthetic directly into the highly cancellous bone. This is especially advantageous in cases of irreversible pulpitis or MIH-affected teeth where inflammation compromises diffusion from conventional infiltration or nerve blocks.[38] The high success rate (88.9%) reported by Dixit and Joshi[30], particularly in the mandible where nerve blocks often less effective underscores its value. Additionally, IO anesthesia offers faster onset and fewer postoperative complications, making it well suited for pediatric patients.

Evidence strongly supports the use of a pre-procedural non-steroidal anti-inflammatory drug (NSAID) such as ibuprofen.[32, 33] Chronic pulpal inflammation in MIH-affected teeth leads to the release of inflammatory mediators such as prostaglandins, bradykinin, which sensitize nociceptors and lower pain thresholds.[39] NSAIDs inhibit cyclooxygenase enzymes, thereby reducing prostaglandins synthesis and inflammation.[40] Administering ibuprofen approximately one hour before the dental procedure can enhance anesthetic efficacy, improve patient comfort and reduces anxiety.

Peedikayil et al.[34] highlighted cryotherapy as a promising, non-pharmacological adjunct. Application of cold reduces nerve conduction velocity, limits inflammatory edema, and provides a counter-irritant effect.[41] While its mechanism alongside local anesthesia warrants further study, its simplicity and non-invasiveness make it an attractive option for managing intraoperative pain in MIH cases.

Unlike other adjunctive therapies, photobiomodulation did not significantly improve local anesthetic success MIH-affected teeth[35]. While PBMT has shown benefits in other dental applications,[42] its specific application as an adjunct to local anesthesia in MIH may not yield the desired synergistic effects, or the parameters used in the study may not have been optimal. Further research with varying parameters and larger sample sizes are needed before definitive conclusions can be drawn.

While the reviewed studies provide valuable insights, certain limitations should be considered. Some studies included relatively small sample sizes, limiting the generalizability of the findings. Variability in study designs, patient populations, and outcome measures complicate direct comparisons. Moreover, the subjective nature of pain perception, especially in pediatric patients, introduces reporting bias.

A major limitation of the present synthesis is the inconsistent reporting of MIH severity among included studies. Most trials focused on teeth with post-eruptive breakdown and did not stratify participants by MIH severity (mild versus severe). As a result, it was not possible to determine whether the efficacy of local anesthesia differs by MIH severity. This gap precludes a definitive conclusion regarding severity-dependent anesthetic performance. Future primary studies should adopt standardized MIH severity classifications (e.g., those defined in established MIH guidelines) and report LA outcomes stratified by severity. Such reporting would allow robust subgroup analyses and a more nuanced understanding of anesthetic needs in MIH cases.

Future research should also prioritize large, multi-center randomized controlled trials using standardized protocols and objective pain assessment tools. Long-term follow-up could assess the impact of these strategies on dental anxiety and treatment compliance. Exploration of other potential adjunctive therapies, such as optimized premedication regimens, and advanced delivery systems may further improve MIH pain management.

CONCLUSIONS

Current evidence supports several strategies for improving local anesthesia outcomes in MIH affected teeth. Articaine 4% should be considered the first-choice anesthetic for MIH-affected teeth, particularly mandibular molars with awareness of possible injection discomfort. Preemptive analgesia with NSAIDs, administered one hour before treatment can reduce pulpal inflammation and enhances anesthetic success. Intraosseous anesthesia serves as a valuable primary or supplemental option, especially for mandibular cases resistant to conventional blocks. Cryotherapy on the tooth surface after nerve block may reduce intraoperative pain and discomfort, particularly in anxious or younger patients. Photobiomodulation currently lacks sufficient evidence for anesthetic enhancement, and future research should focus on large, well designed clinical trials to clarify its role. priorities other evidence-based options. Overall, implementing these strategies can significantly improve pain control, reduce dental anxiety and enhance treatment experiences for children with MIH.

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