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Desensitizing and remineralizing agents used in the hypomineralization of molar incisors in pediatric population

Trabajo de titulación previo a la obtención del título de Odontólogo

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Resumen

Esta revisión tiene como objetivo resumir la evidencia disponible sobre diversos agentes desensibilizantes utilizados en la hipomineralización incisivo molar (MIH) en la población pediátrica. En la MIH, la calcificación y la maduración en la etapa de amelogénesis se ven comprometidas, lo que afecta a la mineralización del esmalte. La MIH afecta a la calidad de vida a través de la hipersensibilidad dental, que es la respuesta de los dientes a estímulos externos, incluyendo cambios de temperatura y presión durante la masticación, afectando a la calidad de vida. Se realizó una revisión bibliográfica en PubMed, Scopus, Science Direct, Scielo y Google Scholar, centrada en la búsqueda de estudios publicados entre 2018 y 2023 cuyos datos se recopilaron y seleccionaron de forma independiente. Se recopilaron un total de 2380 artículos, de los cuales 10 estudios cumplieron los criterios de elegibilidad. Estos estudios se centraron en agentes utilizados para la remineralización y la disminución de la sensibilidad dental. Estos agentes incluyen fosfopéptido de caseína amorfa, dentífricos compuestos de flúor, arginina, hidroxiapatita, barniz de flúor, novamin, nitrato potásico, fluoruro de diamina de plata y láser como método preventivo de la sensibilidad dental. Se ha demostrado que diversos agentes desensibilizantes han tenido un impacto significativo en la remineralización del esmalte, reduciendo la sensibilidad dental. Se requieren más estudios longitudinales para proporcionar planes de tratamiento definitivos y eficaces para los pacientes con MIH.

Palabras clave del autor: sensibilidad dentinaria, defectos de desarrollo del esmalte, hipomineralización incisivo molar, remineralización dental

Abstract

This review aims to summarize the available evidence on various desensitizing agents used in molar incisor hypomineralization (MIH) in the pediatric population. In MIH, calcification and maturation at the amelogenesis stage are compromised, affecting enamel mineralization. MIH affects quality of life through dental hypersensitivity, which is the response of the teeth to external stimuli, including temperature and pressure changes during chewing, affecting quality of life. A literature review was conducted in PubMed, Scopus, Science Direct, Scielo, and Google Scholar, focusing on searching for studies published between 2018 and 2023 whose data were independently collected and selected. A total of 2380 articles were collected, of which 10 studies met the eligibility criteria. These studies focused on agents used for remineralization and tooth sensitivity decrease. These agents include amorphous casein phosphopeptide, toothpastes composed of fluoride, arginine, hydroxyapatite, fluoride varnish, novamin, potassium nitrate, silver diamine fluoride and laser as a preventive method for tooth sensitivity. There has been evidence that various desensitizing agents have had a significant impact on remineralizing enamel, reducing dental sensitivity. More longitudinal studies are required to provide definitive and effective treatment plans for MIH patients.

Author keywords: dentin sensitivity, developmental defects of enamel, molar incisor hypomineralization, tooth remineralization.

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1. Introduction

Koch et al. reported congenital hypomineralization of permanent first molars and permanent incisors in 1970 [1]. This condition was named Molar-Incisor Hypomineralization (MIH) at the European Academy of Pediatric Dentistry (EAPD) Congress in Bergen in 2000 [1]. Accordingly, MIH is a qualitative defect in enamel development, affecting at least one permanent first molar (PMF) and one incisor [2]. Nevertheless, primary teeth, particularly the second primary molar (HSMP) and canines, predict MIH occurrence in permanent teeth. [2,3].

Globally, MIH is prevalent at 14.2%, with a multifactorial etiology [3]. The prenatal stage is influenced by gestational hypertension, urinary infections, antibiotics, antiepileptics, viral infection and fever. Perinatal stage is characterized by low birth weight, intracranial hemorrhage, alterations in calcium and phosphate metabolism, malnutrition, and prolonged births. Conversely, postnatal factors include vitamin D deficiency, gastrointestinal alterations, respiratory problems, chickenpox, rubella, mumps, as well as antibiotics and NSAIDs such as ibuprofen [3,4].

MIH symptoms are well-defined opacities that range in size and magnitude from white, which is less porous and located inside the enamel organ, to yellow-brown, causing alterations both functionally and aesthetically. Despite this, MIH may be misdiagnosed as dental fluorosis, amelogenesis imperfecta, or enamel hypoplasia. (Table 1). [5,6,7].

Histologically, mineral quantity and quality are reduced in enamel affected by MIH [1]. Hydroxyapatite crystals are less compact, disorganized with increased porosity throughout enamel thickness, reduced modulus of elasticity, hardness and increased protein content [1,7]. Due to the thin immersion, there is a posteruptive fracture of the enamel, exposing the dentin subsurface, increasing the possibility of dental biofilm accumulation [1,7]. A high risk of dental caries exists, as microorganism colonies, poorly packed crystallites, and disorganized prisms have been evidenced under electron microscope that easily penetrate hypomineralized enamel surface defects and infect dentinal tubules, causing dental hypersensitivity and subclinical pulp inflammation [1,7]. It has been demonstrated that levels of immune cells and innervation are higher in pulp horns and subodontoblastic regions of molars with HIM compared to healthy teeth; however, e vascularization is equal in both [1].

Histologically, hypomineralization in mild MIH involves only the inner third of the enamel, with the outer two-thirds intact [8]. As opposed than mild MIH, severe MIH affects the entire enamel layer, resulting in disorganized crystals that are less compact and have low calcium and phosphate ions [9]. Thus, an updated coding has been implemented that grades MIH severity from 0 to 10, which facilitates treatment decisions (Table 2) [8].

Dental hypersensitivity to different stimuli, whether chemical, mechanical, or thermal, occurs in MIH patients when mechanical removal of biofilm or inspiration of air occurs [2]. This condition is, however, dependent on its severity [2]. Being more prevalent in moderate and severe MIH, it can interfere with local anesthesia's mechanism of action, leading to failure in different treatment plans due to increased pain, causing fear and anxiety [2]. Hypersensitivity increases dental biofilm accumulation, causing dental caries, coronary destruction, and even tooth loss (Table 3) [2].

In accordance with hydrodynamic theory, external stimulus move dentinal tubular liquid, stimulating the pulp area's nerve processes and causing pain [2]. Heat expands and displaces the liquid inside the dentinal tubule; cold and touch act induce pain inversely [2]. It is believed that the intradental myelinated Aβ fibers and some Aσ fibers that send terminals to dentinal tubules respond to the movements of the liquid inside the tubule, which produces short, sharp pain [2].

TABLE 1. Differential diagnosis of MIH [10,11].

MIH [10]	**DENTAL FLUOROSIS** [10]	**AMELOGENESIS IMPERFECTA** [11]	**ENAMEL HYPOPLASIA** [11]
Associated with systemic alterations. Qualitative defects.	Associated with excessive ingestion frequency of fluoride compounds during dental mineralization.	Associated with hereditary and genetic factors, clinical history helps us determine the cause.	Associated with systemic, environmental and genetic factors. Primary teeth may develop defects due to trauma or infection. Quantitative defects.
Well-demarcated opacities ranging from white to yellow-brown with enamel more prone to fracture.	Diffuse opacities that clinically range from diffuse and irregular white lines to loss of structure with marked discoloration.	Teeth turn yellow, resulting in softer and thinner enamel.	They appear in grooves, small cavities or enamel may be partially or completely absent.
It affects permanent incisors and molars.	It affects both the deciduous and	It affects deciduous and permanent teeth.	It affects a single tooth or a small group of

	permanent dentition during development.		adjacent teeth.

TABLE 2. Codes of the molar-incisor hypomineralization severity scoring system and their descriptors [8].

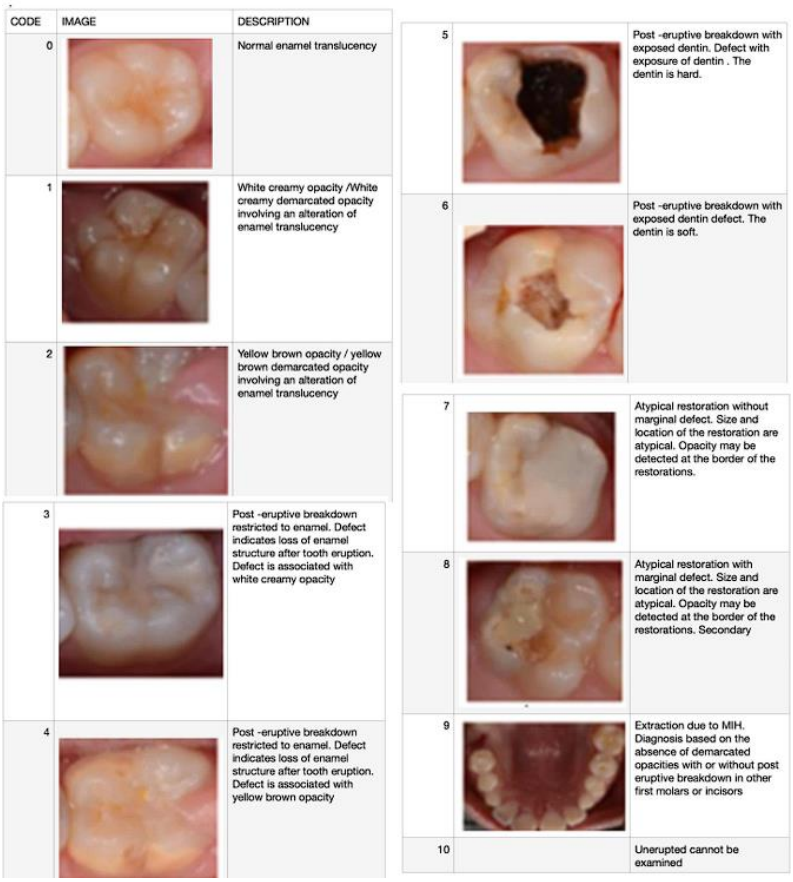

TABLE 3. Diagnostic criteria for MIH by the European Academy of Pediatric Dentistry (EAPD) [12].

Criteria	Description
Teeth involved	● A minimum of one of the four FPM. ● Permanent incisors may also be affected at the same time. ● The more affected the molars are; the more incisors involved and the more serious the defects. ● Defects can also be seen on the primary second molars, premolars, permanent second molars, and canines tips.

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Demarcated opacities	● Demarcated opacities present with an alteration enamel translucency. ● Variability in color, size, and shape. ● White, creamy, or yellow to brown. ● Only defects greater than 1 mm should be considered.
Posteruptive enamel fracture	● Severely affected enamel breaks down after tooth eruption due to chewing forces. ● Loss of the initially formed surface and variable degree of porosity of remaining hypomineralized areas. ● Pre-existing demarcated opacity often contributes to the loss. ● Areas of exposed dentin and subsequent caries development.
Sensitivity	● Affected teeth usually display sensitivity, ranging from mild responses to external stimuli to spontaneous hypersensitivity. ● MIH molars may require alternative anesthetic techniques or anesthesia delivery adjustments.
Atypical restorations	● Size and shape of restorations are not conforming to the typical caries picture. ● Restorations in molars extend to the smooth buccal or palatal/lingual surfaces. ● Opacity is frequently observed at restoration margins.
Molar extraction due to MIH	Molars can be considered extracted by MIH when: ● Relevant notes in the records. ● Delimited opacities or atypical restorations on the other first molars ● Incisors with typical demarcated opacities

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1.1 Desensitizing Agent Options for Teeth Affected by MIH

1.1.1 Amorphous caseinate-calcium phosphate phosphopeptide (CPP-ACP):

CPP is a peptide derived from casein that forms milk protein nanocomplexes [13]. It binds to calcium and phosphate ions through phosphoryl residues and stabilizes them as ACP, providing minerals to the oral environment [14]. Acidic pH releases them, while alkaline pH reserves them [14].

CPP-ACP anticariogenic mechanism involves depositing amorphous calcium phosphate on tooth, maintaining a supersaturated solution in the dental enamel, so that in sites of pH 5.5 or lower (caused by bacterial metabolism), which causes H ions to react with crystals of the phosphate group of the dental enamel, converting the PO4 ion into HPO4 [13,14]. Therefore, action of CPP-ACP reduces demineralization and increases mineralization, it exerts an antibacterial action, preventing biofilm adhesion to the tooth surface, attenuating the growth of Streptococcus sobrinus and Streptococcus mutans [13,14].

Conversely, CPP-ACP inhibits dentin hypersensitivity by occluding the dentinal tubules by the bioavailability of calcium and phosphate in saliva, which forms part of the composition of toothpastes like Mi Paste® at 10%, Mi Paste Plus at 10% CPP-ACP and 0.2% NaF (900 ppm F) that should be applied for 2 minutes on the surface of the teeth and after 30 minutes the patient can consume food [14].

1.1.2 Toothpaste composed of 8% Arginine.

Arginine is a positively charged amino acid, obtained from food, with a pH of 6.5 to 7.5, which resists acids derived from the diet and promotes dentinal tubule closure. Among its chemical components are calcium, phosphorus, oxygen along with a small amount of carbon and nitrogen [15]. Hence, toothpaste containing 8% arginine is recommended at least twice daily to reduce dental sensitivity, as it seals dentinal tubules by adhering to their walls. Due to arginine’s alkalinity, dental pain’s hydrodynamic mechanism is avoided [15].

1.1.3 Hydroxyapatite pastes

Increasingly, patients with phosphoric acid deficiencies are offered hydroxyapatite-based toothpastes [16]. Hydroxyapatite, a naturally occurring element that is found in bones and teeth, induces remineralization of affected surfaces by MIH by chemically bonding to natural apatite crystals, since the enamel surface is porous, allowing hydroxyapatite particles to

penetrate more deeply, strengthening the growth and integrity of crystals by attracting calcium and phosphate ions [3]. The nanoparticles in hydroxyapatite-based pastes that are encountered on the tooth surface facilitate sealing of the dentinal tubules, prevent stimuli from reaching the pulp, restoring mineral density and eliminating tooth sensitivity, thus eliminating pain [16,17].

1.1.4 5% Sodium Fluoride Varnish

It is a remineralizing agent on the HIM that acts for a prolonged action (4 months), containing 22600 ppm of fluoride ion (5. 65mg) and tricalcium amorphous phosphate [18]. As for its mechanism of action, fluoride acts in conjunction with saliva to form calcium fluoride (CaF2) in the enamel as a secondary response after its application to teeth surfaces [18]. This causes a decrease in the plaque pH, then CaF2 dissolves and releases fluoride ions [18]. By prolonging release, it decreases demineralization, inhibits bacteria, and favors remineralization [18].

This technique involves applying it once a week for three or four weeks to the teeth affected with MIH. First, we clean and dry the teeth, followed by applying a thin layer of fluoride with the help of a brush in relative isolation. Patients / representatives should be instructed not to eat anything for at least 2 hours after the procedure. Additionally, it is recommended to suspend brushing for that day or rinse with some kind of solution [19,20].

1.1.5 Silver Diamine Fluoride (SDF)

FDP reacts with hydroxyapatite on the tooth surface, forming silver phosphate and calcium fluoride [21]. When the compounds of silver oxide and silver phosphate react, the lesions turn black, which is why it used to prevent and treat caries caused by *mutans streptococcus* [22]. This causes remineralization and reduces enamel and dentin demineralization. It inhibits collagen matrix destruction by inhibiting collagenase [21,22]. This material is indicated for cases of dentine caries that do not involve the dental pulp, in both dentitions for both anterior and posterior teeth, for non-cooperative patients and children with limited access to dental care [23]. FDP is presented at 12%, 30%, and 38% [22]. Its is recommended to apply the product in relative isolation and to use a micro brush to apply a drop every three teeth for 30 to 60 seconds at a time interval every 4, 6, or 12 months [22]. In addition, it creates precipitates of calcium phosphate, calcium fluoride, and silver reaction products that seal these tubules. By blocking stimulus transmission, hypersensitivity is reduced or eliminated [17].

1.1.6 Novamin

Calcium, sodium, phosphorus and silicate comprise this synthetic mineral [2]. A bioactive glass particle with a size of 18 um is used as an active restorative agent [2]. This material aids in remineralizing dentinal tubules through apatite formation [2]. In turn, this reduces fluid permeability and decreases dentin hypersensitivity [2]. Novamin-containing toothpastes have a better remineralization capacity than CPP-ACP, since the latter adheres more compactly to the enamel surface [2].

As a result of sodium release, the pH rises, calcium-phosphorus complexes are formed, along with ions in saliva, and calcium-phosphate (Ca-P) layer layer is formed on the tooth surface [2]. Carbonated calcium hydroxyapatite crystals are formed as the reaction's advances [2].

1.1.7 Potassium nitrate 5%.

Within minutes after application, it diffuses rapidly into the enamel and dentin towards the pulp, blocks stimulus transmission, and depolarizes the nerve surrounding the odontoblast process, preventing it from repolarizing [12]. This reduces nerve excitability and pain transmission [12]. The formulations of dentifrices, desensitizing gels, and some whitening products contain potassium nitrate, which has an almost anesthetic effect on the nerve fibers [12].

1.1.8 Diode Laser

Recently, lasers have gained popularity as a treatment method in this area. Dentin hypersensitivity can be effectively treated with an 810 nm diode laser alone or in combination with sodium fluoride gel[12]. By blocking painful stimuli transmission from the dentinal tubules to the central nervous system, it desensitizes the sensory nerves [12]. The nerve impulse in the dental pulp is altered rather than exposed dentin. The suppression of the nerve impulse is due to the blockade of depolarization of afferent C-fibers [12]. Laser treatment was chosen for its therapeutic effects on pain and inflammation without altering enamel, dentin, or pulp tissue morphology [12].

This study aims to conduct a literature review by searching multiple sources of information to determine the type of desensitizing agent used in pediatric molar incisor hypomineralization.

2. Materials and methods

We analyzed the digital databases PubMed, Scielo, Google Scholar, Science Direct, and Scopus by combining the DeCS/MeSH keywords. The PRISMA (Preferred Reporting Items for Systematic Headings) guideline was used for this literature review. The research protocol

was registered in the PROSPERO international database (Registration ID: CRD42024524945).

2.1 Eligibility criteria

- Controlled clinical trials.
- Literature Reviews
- Meta-analysis.
- Systematic reviews
- Articles in English and Spanish published between 2018 and 2023.
- Full-text articles available.
- Clinical cases

2.2 Exclusion criteria

- Studies unrelated to dentistry.
- Articles older than five years were avoided.

2.3 Search terms

Search terms were derived from previous scientific articles. The keywords used were: Dentin sensitivity, developmental defects of enamel, molar incisor hypomineralization, tooth remineralization and Boolean operators AND/OR, based on DeCS/MeSH keywords combination.

Search strategies are listed below (Table 4):

TABLE 4. Search strategies used in different databases.

Database	Search strategies
PubMed/Medline	((((Molar Incisor Hypomineralization) AND (Dentin Sensitivity)) OR (Developmental Defects of Enamel)) OR (Tooth Remineralization)
Google Scholar	“Molar incisor hypomineralization” AND “tooth remineralization” AND “Dentin Sensitivity” AND “Developmental Defects of Enamel”
Scielo	((Defectos del Desarrollo del Esmalte)), ((Hipomineralización incisivo Molar)), ((Sensibilidad Dental)),((Remineralización Dental)).
SCOPUS	molar AND incisor AND hypomineralization AND dentin AND sensitivity

	OR developmental AND defects AND of AND enamel OR tooth AND remineralization
SCIENCE DIRECT	molar AND incisor AND hypomineralization AND dentin AND sensitivity OR developmental AND defects AND of AND enamel

2.4 Data collection

Article titles, publication dates, and article designs were analyzed. After reviewing the articles' titles, we selected those that met our selection criteria. Following the analysis of the summaries of the remaining articles, we excluded those that did not meet the selection criteria. As a final step, the full text of the remaining articles was reviewed for accuracy (Table 5).

3. Results

3.1 Search strategy

2380 articles were found, of which those that did not meet the inclusion criteria were excluded. Among the remaining studies, 30 articles were evaluated in detail. The final selection consisted of 10 articles on desensitizing agents used in molar incisor hypomineralization. Prisma flow chart (Figure 1) illustrates the entire process.

(Se excluyeron por el motivo de que las diferentes bases de datos se encontraban los mismos artículos y no aportaban información relevante.)

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TABLE 5. Main characteristics of the included studies.

Author (year)	Objective	Type of study	Population (n)	Intervention and comparison	Results	Study conclusion
Almuallem Z et al. 2018 [25]	To highlight the most important aspects of MIH, from its prevalence to treatment options.	Literature review	Does not apply	Effectiveness of CPP-ACP with Novamin in remineralization of MIH teeth.	NovaMin-containing toothpastes remineralize teeth better than CPP-ACP-containing toothpastes in MIH teeth with HIM.	MIH teeth can be managed with remineralization techniques. However, these treatment modalities require further investigation to introduce the best technique/protocol in MIH cases.
Amaechi 2022 [3]	Compare fluorine-free hydroxyapatite-based pastes effectiveness with a fluorinated paste in the	In situ study	15 subjects between 18 and 60 years old.	They used enamel blocks with MIH lesions. Group 1: 30 blocks of hydroxyapatite. Group 2: 30 blocks of fluoride paste.	The fluorine-free hydroxyapatite paste showed a significant percentage as opposed to the fluorinated paste.	The study showed that hydroxyapatite-based paste significantly remineralized teeth with HIM relative to fluoride-based paste.

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	remineralization of MIH pieces.			Time 14 days for both groups.		
Al-Nerabieah 2024 [23]	To compare the efficacy of silver diamine fluoride (SDF) and calcium phosphate amorphous calcium phosphopeptide casein fluoride varnish (CPP-ACPFV) in preventing enamel deterioration and sensitivity in molars affected by	Randomized controlled trial	A total of 100 children aged 6 to 9 years were enrolled in the study with two contralateral permanent molars mildly affected by MIH.	Affected molars were randomly and equally assigned to receive either SDF or CPP-ACPFV treatment. The interventions were applied at four different time points (baseline, 3, 6, 9 months), and the incidence of caries, caries progression, enamel breakdown, and sensitivity were	However, no significant differences were observed in enamel breakdown scores between the treatment groups, as the majority of teeth in both groups exhibited a score of 0. Furthermore, there were no significant differences in sensitivity between the treatment groups throughout the study	Both interventions showed promise in preventing enamel breakdown and improving sensitivity.

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	molar incisor hypomineralization (MIH) in children.			assessed.	period.	
Butera 2023 [24]	To evaluate zinc hydroxyapatite-based paste effectiveness on MIH teeth.	Randomized clinical trial	25 subjects were of an age range between 6 and 10 years	A hydroxyapatite-based paste was assigned for home use. The application occurred in a single quadrant for the respective comparison.	Mild lesions and dental sensitivity decreased significantly in MIH teeth.	The paste showed a desensitizing effect on teeth affected by mild MIH.
Camargo 2023[2]	To describe the therapeutics available as desensitizers in HMI through a review of the	Literature review	Does not apply.	Does not apply	Most studies concluded that the use of various agents such as fluoride varnish, 8% arginine pastes, CPP-ACP	Current evidence from clinical studies indicates that several approaches may be effective in remineralization and

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	literature.				(casein phosphopeptide-amorphous calcium phosphate) based pastes, laser use, should be incorporated in patients with IMH, however, the evidence is scarce.	desensitization of HMI-affected teeth, including regular daily care with a traditional fluoride toothpaste, or with an arginine-containing toothpaste and the use of fluoride varnishes or CPP-ACP pastes.
Cardoso 2022 [28]	To evaluate the in vitro application of CPP-ACP in the transition and hypomineralization areas of white and yellow MIH opacities.	In vitro study	Extraction of 15 severely hypomineralized molar teeth.	Group A: 14 opacities of 10 hypomineralized teeth with white opacities treated with CPP-ACP remineralizing agent. Group B: 14 opacities of 5 hypomineralized teeth with yellow opacities treated with CPP-	Statistically significant increases in mineral density in the hypomineralized and transition areas of the enamel after CPP-ACP treatment in white and yellow opacities.	Significant increase in the physical strength of MIH-affected enamel after topical application of CPP-ACP, which may be due to an increase in mineral content in yellow and white stains.

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				ACP remineralizing agent		
Kumar 2022 [27]	To assess and compare the effects of a cream based on CPP-ACP and fluoride varnish on the remineralization of MIH teeth.	In situ and in vitro study	30 subjects, 11 men and 19 women, ranging in age from 8 to 16 years.	First study group: single daily CPP-ACP cream application. Second study group: Fluoride varnish every three months.	No significant differences were found in mineral content increase.	After 6 months of application, it was concluded that fluoride varnish and CPP-ACP are equally effective at remineralizing MIH teeth.
Lygidakis 2022 [12]	Update the clinical guidelines for dentists treating children with HIM.	Clinical guide	Does not apply	Etiological factors and treatment options for MIH teeth.	The etiology is still multifactorial, and treatments depend on diagnosis and planning.	All treatment plans are effective for MIH teeth. However, more long-term research is needed to provide the correct treatment plan.

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Meza 2020 [19]	Employ fluoride varnish in patients with MIH.	Observational, longitudinal, prospective study	Subjects range from 6 to 15 years old.	Fluoride applications every six weeks and six months.	High results in remineralization, returning teeth' properties.	Fluoride applications in the early stages of MIH teeth had a remineralizing and practical effect on the patient.
Muñiz 2020 [26]	Investigating low level laser therapy (LLLT) associated with fluoride varnish for desensitization of MIH teeth.	Randomized clinical trial	66 children aged 6 to 12 years and a total of 214 teeth with a sensitivity score ≤3.	Efficacy of low-level laser therapy associated with fluoride therapy for desensitization in MIH teeth.	Combining laser treatment with exclusivity demonstrated significant desensitizing effects after initial administration, proving laser's immediate effect.	Fluoride varnish and the combination of treatments led to greater desensitizing effect on MIH teeth. Laser therapy demonstrated an immediate desensitizing effect, while fluoride varnish had a delayed effect.

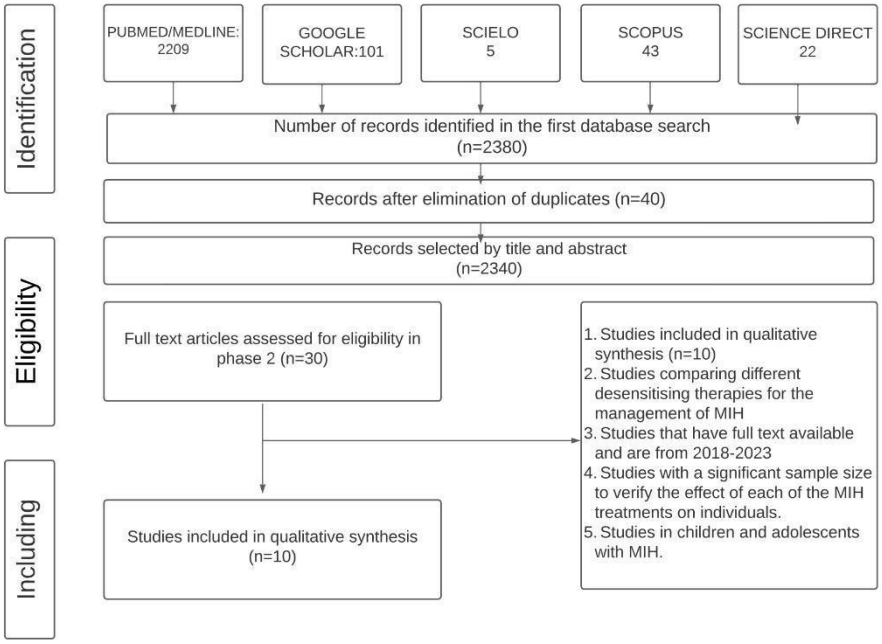

FIGURE1. Prisma flowchart of the review selection process.

4. Discussion

Molar incisor hypomineralization (MIH) refers to a qualitative developmental defect that occurs rapidly in the molar incisors, leading to a wide range of dental complications, including caries lesions, aesthetic defects, occlusion changes as a result of early tooth loss, and hypersensitivity of the teeth. Patients' quality of life can be significantly affected by this condition, so an efficient and correct diagnosis is essential for decision making either in a preventive plan that reduces the risk of caries. Increasing dental tissue conservation or a restorative treatment plan. From this, promote methods such as remineralizing agents that increase the mineral density of the enamel, improving properties such as resistance to fracture, thus avoiding hypersensitivity and cavities development.

Almuallem et al. [25] Casein phosphopeptide calcium phosphate phosphate-amorphous casein phosphopeptide phosphine (CPP-ACP) can be used long-term in the early stages where the surface enamel of newly erupted teeth is not fully mature. This increases calcium and phosphate bioavailability within the saliva, promoting remineralization and desensitization of MIH teeth. Due to its CPP content, it also binds strongly to biofilms on teeth. Consequently, the ions are prevented from precipitating spontaneously and can penetrate deeper into the subsurface lesion. By contrast, fluoride products remineralize only the surface layer. A combination of fluoride and CPP-ACP has been shown to be more beneficial than either agent alone. This study confirms *Cardoso et al.* [28]'s in vitro study on 15 extracted teeth which found

that CPP-ACP increased mineral density in hypomineralized areas in both white and yellow opacities. Furthermore, enamel hardness in teeth with MIH that have white opacities improved significantly after CPP-ACP application for 28 days improving their structural and mechanical characteristics.

However, despite the lack of studies, *Allmuallem et al. [25] and* Camargo et al. *[2]* report that Novamin paste is an active restorative agent that improves remineralization and reduces hypersensitivity. It mineralizes the small holes in the dentin, decreasing sensitivity. Due to NovaMin's compact attachment to enamel, toothpastes containing NovaMin have a higher remineralization capacity than CPP-ACP.

Amaechi, et al. [3] conducted an in situ study to assess the efficacy of remineralizing agents between fluoride varnish and hydroxyapatite paste in increasing mineral content in teeth affected by MIH in which fluoride varnish contains 5% sodium fluoride. As one of the most used materials, it contains 22600 ppm of fluoride and amorphous tricalcium phosphate. The fluoride hydroxyapatite forms when it interacts with crystals of hydroxyapatite to create fluoride hydroxyapatite, which reduces dental hypersensitivity while maintaining enamel properties. While fluoride-free hydroxyapatite particles, which are biocompatible and biomimetic, are found in oral hygiene products such as toothpastes and mouthwashes, promoting caries remineralization and therefore decreasing its progression. which prevents through two mechanisms. First, hydroxyapatite particles are deposited in the microporosities of demineralized tissue, promoting the deposition and growth of crystals which promote the continued attraction of calcium and phosphate ions from the surrounding remineralization solution . Secondly, hydroxyapatite particles could dissolve in bacterial biofilms, which lead to higher levels of calcium and phosphate ions on the tooth surface. Accordingly, hydroxyapatite without fluoride is much more desensitizing than fluoride varnish. It is in agreement with a randomized clinical trial by *Butera et al.* [24], which reported that hydroxyapatite in paste form had a great desensitizing effect, resulting in fewer treatments needed in patients with MIH. With its easy home use and short application time, it improves enamel integrity and reduces tooth sensitivity.

Kumar *et al.* [27] conducted an in situ study to evaluate and compare the effect of CPP-ACP cream and fluoride varnish on remineralization in teeth with MIH. CPP-ACP has the advantage of being easy to use at home after 6 months of application, while both treatments have the same remineralization effectiveness. Therefore, no clinic intervention is required. Since fluoride varnish has a greater prevention and desensitizing effect than CPP-ACP cream, it is more profitable. Agreeing with a longitudinal, prospective study on MIH patients aged 6 to 15

years conducted by Meza et al. [19]. Fluoride varnish was applied to teeth for 6 weeks, followed by a 6-month period, preventing tooth erosion due to enamel preservation. Therefore, dental sensitivity decreased significantly.

Al-Nerabieah et al. [23] in a randomized controlled trial compared the effectiveness of SDF and calcium phosphate amorphous calcium phosphopeptide casein fluoride varnish (CPP-ACPFV) which demonstrated an improvement in sensitivity, with no significant differences observed between the two groups sensitivity scores were recorded at 3, 6, 9 and 12 months from baseline, This indicates that both materials were effective in alleviating the sensitivity commonly associated with MIH, however it should be noted that silver fluoride has presented several drawbacks such as irreversible dark staining at the restoration margins and cavitated lesions.

The best clinical practice guidelines updated by Lygidakis et al. [12] mention that all available treatments counteract sensitivity. However, there have been no studies evaluating the effectiveness of desensitizers in teeth with MIH involving larger long-term sample sizes.

Conclusions

MIH is a multifactorial dental anomaly that negatively impacts patients' quality of life due to sensitivity and dental caries. Hence, precision, correct clinical diagnosis, and patient collaboration are essential to a successful treatment plan. This study has shown several treatment options for teeth with MIH, including fluoride pastes or varnishes (remineralization due to the advantage of having a prolonged release source), pastes containing arginine with the positive effect of adhering and closing the dentin tubules (preventing dental hypersensitivity), and CPP-ACP, which promotes remineralization by repairing apatite crystals and producing dentinal tubule occlusion, thereby decreasing hypersensitivity. To prevent and treat MIH, hydroxyapatite and casein were used, as well as silver diamine fluoride, which inhibits collagen degradation and promotes remineralization. However, Fluoride is widespread in both dental clinics and oral hygiene products In various studies with large sample sizes, optimal remineralization effects and decreased sensitivity have been reported.

Longitudinal studies with a good scientific basis are required to identify in the long term the best gold standard desensitizing agent using minimally invasive techniques that do not adversely affect oral and systemic health, thereby inproving functional, aesthetic, and psychosocial aspects of dentistry.

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