Does MIH Affects Preoperative and Intraoperative Hypersensitivity?

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Objective: *Hypersensitivity is an important problem that is encountered during the treatment of hypomineralized teeth. The aim of this prospective study was to compare responses to electrical pulp tests (EPTs) and cold tests among carious teeth with and without molar incisor hypomineralization (MIH) before and after the administration of local anesthesia for caries removal* ***Results:*** *The EPT results of anesthetized carious teeth without MIH were significantly higher than those of carious teeth with MIH ($p = 0.011$). The cold test results were significantly higher for anesthetized carious teeth with MIH than for those without MIH ($p = 0.0001$). Intraoperative pain was significantly higher for carious teeth with MIH ($p = 0.003$).* ***Conclusions:*** *The results of this study suggest that even after achieving sufficient anesthesia, hypersensitivity remains a clinical problem in MIH-affected carious molars. The results presented in this study indicate that this phenomenon is not related to achieving effective local anesthesia; therefore, behavior management in such cases is of the utmost importance compared to relying on adjacent anesthetic methods.*

Keywords: *Carious Teeth, Cold Test, Electrical Pulp Test, Hypersensitivity, Molar Incisor Hypomineralization*

INTRODUCTION

The term "molar incisor hypomineralization (MIH)" describes "hypomineralization of systemic origin of one to four permanent first molars, frequently associated with affected incisors", and this phenomenon has an unclear multifactorial etiology. Several conditions may act together and increase the risk of MIH additively or even synergistically. These factors are genetics, antibiotics (i.e., amoxicillin), potential toxic agents (i.e., chemotherapy), prenatal or postnatal medical issues, childhood diseases and environmental factors. One or a combination of these factors might affect the basic developmental stages of ameloblasts during odontogenesis of the incisor and first permanent molar teeth.[1-5]

MIH can be diagnosed with different clinical features, such as demarcated opacities at occlusal and buccal parts, enamel disintegration, atypical restorations, tooth sensitivity, or early extractions. The defects vary in size and color from white, creamy, and yellow to brown. The severity of the defects is recommended to be recorded as mild or severe. In mild cases, demarcated enamel opacities with occasional sensitivity to external stimuli are present without enamel breakdown. There is usually no sensitivity to tooth brushing. In severe cases, demarcated enamel opacities and enamel breakdown are present. Caries, persistent/spontaneous hypersensitivity affecting function and strong aesthetic concerns are commonly observed in severe cases.[3-6]

Hypersensitivity of teeth with MIH may range from a mild response to external stimuli to spontaneous hypersensitivity.[3] Children with MIH often report sensitivity to a variety of normal innocuous thermal, mechanical, and osmo-chemical stimuli. During dental procedures, difficulties in achieving adequate analgesia for restoration are occasionally encountered.[5,7-9] Reviews and clinical management statements underline this issue; however, to the best

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of the authors' knowledge, no randomized clinical trial has investigated it.[5,9] Research has focused on the possible pathophysiological mechanisms behind this phenomenon which, in turn, have not been determined. Fagrell *et al*.[10] showed that bacterial invasion is seen even with the intact enamel of MIH teeth, suggesting that hypomineralized enamel acts as an open door for oral bacteria to penetrate through the dentinal tubules and create subclinical inflammatory reactions in the pulp. Tissue inflammation may, in turn, lead to morphological and cytochemical changes within sensory neurons, resulting in sensitization of these nerve fibers.[8,10-12]

The aim of this prospective study was to test whether carious teeth with MIH are still hypersensitive, despite being anesthetized as effectively as carious teeth without MIH. Therefore, the authors compared the responses to EPT and cold test results among carious teeth with MIH and without MIH before and after the administration of local anesthesia for the removal of dentine caries. Caries-free teeth with MIH and without MIH were also subjected to the tests as controls. The hypotheses of this study were twofold: (i) when caries is present, teeth with MIH will have lower EPT and higher cold test responses before and after the administration of local anesthesia compared to carious teeth without MIH. (ii) Carious teeth with MIH will have lower initial EPT and higher initial cold test responses than caries-free teeth with MIH.

MATERIALS AND METHOD

This prospective clinical study was approved by the University Medical and Health Sciences Research Board and Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained. An *a priori* test revealed that a total sample size of 48 (24 per group) was required to achieve a power of 0.90 with an effect size of 0.8 and an α error of 0.05. In anticipation of dropouts, we decided to enroll 25 cases per group.

Study Design

The initial study sample was composed of 45 healthy patients with 77 first permanent molar teeth who were referred to the Başkent University, Faculty of Dentistry, Department of Pediatric Dentistry clinic for routine control or dental treatments. The participants were healthy, and their age ranged from 6-12 years. The patients were initially categorized for their anxiety level with the Modified Frankl Scale, and patients with Ratings 4 and 5, which means 'positive' and 'definitely positive', respectively, to accept the treatments, respectively, were included in the study.[13]

Clinical and radiographical assessment, radiographic caries level, International Caries Detection and Assessment System (ICDAS) scores and level of MIH levels were recorded for all included teeth prior to the interventions. Radiographic caries depth was determined with digital periapical radiographs (Image Plate System, Digora®, Soredex, Helsinki, Finland), and dentine caries involved between the outer 1/3 and inner 1/3 of the dentine tissue irrespective of enamel breakdown were included in the study.

The caries status of the teeth enrolled was also scored with ICDAS scores. The ICDAS classification criteria and associated estimates of caries activity is based upon the histological extension of lesions spreading into the tooth tissues. Accordingly, caries was classified with ICDAS scores of 0-6, which were 1-2 for initial-stage caries, 3-4 for moderate caries and 5-6 for extensive caries.[14-18]

The teeth enrolled in the study were also classified using the MIH index proposed by Ghanim *et al*[19]. The classification for MIH ranges from 0-7 and can be defined as no visible enamel defect, enamel defect non-MIH, white creamy demarcated/yellow or brown demarcated opacities, post eruptive enamel breakdown, atypical restoration, atypical caries, missing because of MIH and cannot be scored as 1, 2, 3, 4, 5, 6 and 7, respectively. MIH teeth with atypical carious lesions generally have moderate or extensive caries; therefore, carious teeth with MIH at ICDAS scores of 3/4/5/6 were enrolled in the study for the standardization of the included teeth. Teeth having only post-enamel breakdown without caries were excluded. The carious teeth without MIH were only carious without any hypomineralized areas. The inclusion criteria for ICDAS, MIH level and radiographic caries depth and the distribution of teeth in all groups are shown in Table 1. All teeth enrolled were completely free of irreversible pulpitis signs and symptoms.

The study was conducted in a double-blind manner, and the examiner for the EPT and cold test and the restorative treatment operator were different. A total of 7 patients dropped out from the research on their own will after the initiation of the operatory protocol. A total of 50 carious permanent first molar teeth, 25 with MIH and 25 without MIH, were included in the study. As per the controls, 10 patients with 20 caries-free teeth (10 with MIH and 10 without MIH) were included in the study. The distribution of the groups and the study flowchart are shown in Figure 1.

Preoperative measurements

EPT devices have a rheostat that shows the relative amount of current applied on various scales, such as 0-10, 0-15 and 0-80. In the present study, an analog electrical pulp tester (Pulp Vitality Tester, Parkell, New York, USA) was applied, which increased the current rate from no (0) output to maximum output (10). The receiver probe of the analog electrical pulp tester was placed on the middle third of the buccal surface, and the number with initial sensation was recorded. As per the cold test, refrigerant material (Ice Spray, Artsana, Pozzo D'Adda, Italy) was sprayed on a cotton pellet and rapidly placed on the middle third of the buccal surface until the patient responded within accordance with the instructors within a maximum of 5 seconds.[20]

Treatment Procedure

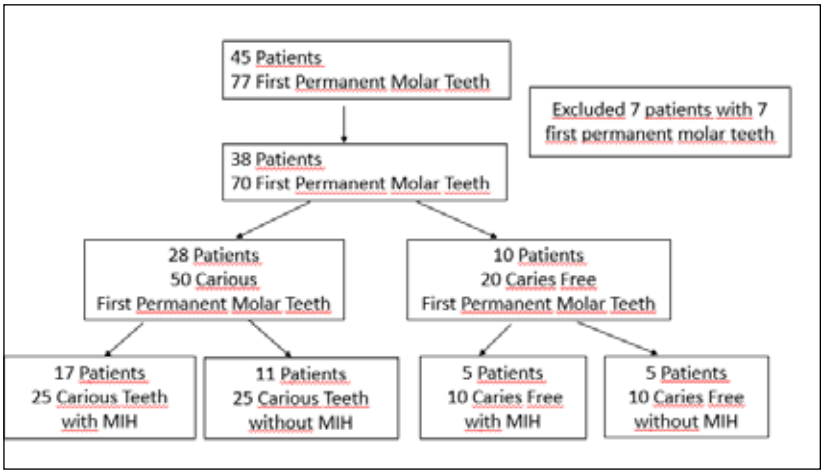
Following the recording of the ICDAS, MIH levels and caries depth, one pediatric dentist presented instruments and materials using the tell-show-do behavior management technique. Next, another pediatric dentist performed the EPT and cold test before and after the administration of nervous alveolaris inferior block anesthesia for mandibular molar teeth or nervous alveolaris superior posterior block anesthesia for maxillary molar teeth. The tests were applied following the confirmation of numbness after approximately 4 minutes.[21] Before the administration of block anesthesia, topical anesthetic spray (Vemcaine 10% Pump Spray, Vem, Turkey) was applied for one minute by a cotton pellet per administration. Additionally, the operator administered the anesthetic solution with a 2-ml plastic disposable syringe with 27-gauge needles in approximately 60 seconds.

The Visual Analog Scale for Pain was used to evaluate (i) the cold tests before and after local anesthesia with 4% Articaine with 1:100,000 epinephrine (Ultracaine® D-S Forte ampule,

Table 1: Inclusion criteria and distribution of the groups

Groups	Inclusion criteria		
	MIH	ICDAS	Radiographic caries depth
Caries with MIH	5 (I, II, III)	3/4/5/6	Inner 1/3 and outer 1/3 dentine
Caries without MIH	0	3/4/5/6	Inner 1/3 and outer 1/3 dentine
Caries free with MIH	2 (I, II, III)	0	NA
Caries free without MIH	0	0	NA

Figure 1. Flowchart of the study



Sanofi-Aventis, Germany) and (ii) pain during the caries removal procedures.[22,23] The control readings for the EPT and cold tests in carious (25 with MIH and 25 without MIH) and caries-free teeth (10 with MIH and 10 without MIH) were applied three times, and the average of the results was used as the final score.

In the teeth receiving the restorative protocol, all cavities were restored with composite resin restorations (Filtek Z250, 3 M ESPE, St. Paul, Minnesota, USA). If any patient reported unbearable pain during the treatment procedure, adjunct methods were used, and the patient was excluded from the study.

Statistical Analysis

The data were analyzed with SPSS V. 21. The Shapiro-Wilk test was used for the number of units while investigating variables with a normal distribution. When interpreting the results, 0.05 was set as the level of significance. The Mann-Whitney U test was used in the analysis of the differences between the groups in the case of variables that did not have a normal distribution. The difference between the dependent variables that did not have a normal distribution was examined by the Wilcoxon signed-rank test.

RESULTS

Demographic data analysis

The study was conducted with 28 patients with 50 carious teeth and 10 patients with 20 caries-free teeth (Figure 1). The average ages of patients in the carious and caries-free groups were 8.9 and 10.02 years, respectively. The sex distribution for the MIH and without MIH groups in carious teeth was 48% and 40% male, respectively. The gender distributions for the caries-free groups with MIH and without MIH were 60% and 50% male, respectively.

ICDAS scores were significantly different between the groups, and the average value for the carious with MIH group was significantly higher ($p = 0.011$). According to the evaluation of numbness in the lip, cheek, and tongue and checking gingival numbness with a fine-tipped probe, all anesthetized teeth had analgesia 100%.

Analysis of the initial EPT and cold test results for all teeth

The initial EPT results did not show any significant difference between the groups ($p > 0.05$). The initial EPT results for caries-free teeth with MIH were higher than those for carious MIH teeth but were not significant. The results also showed that initial EPT scores were numerically the highest for caries-free teeth without MIH (Table 2).

Unlike the EPT scores, there was a significant difference between groups for the initial cold test results ($p < 0.05$). The results for carious teeth (either with or without MIH) were significantly higher than those for caries-free (either with or without MIH) teeth ($p < 0.05$). However, there was no significant difference between carious teeth with MIH and those without MIH. Additionally, there was no significant difference between the caries-free teeth with MIH and caries-free teeth without MIH groups (Table 2).

Comparison of initial and second EPT and cold test results for carious teeth with MIH and without MIH

According to the results, second EPT values were significantly higher in carious teeth without MIH than in carious teeth with MIH ($p = 0.011$). In the evaluation of carious teeth in the MIH group, the second EPT values were significantly higher than the initial EPT values ($p < 0.05$). The second EPT values (the EPT values of

anesthetized teeth) were significantly higher in the carious teeth without MIH group than the initial EPT values ($p < 0.05$) (Table 3).

The second cold test scores were significantly higher in carious teeth with MIH than in carious teeth without MIH ($p = 0.0001$). The first cold test values were significantly higher than the second values for MIH teeth in the carious group ($p < 0.05$). The first cold test values were significantly higher in the carious teeth without MIH group ($p < 0.05$) (Table 3).

Analysis of the intraoperative pain results among the groups

When considering the 10/10 EPT score as unresponsive following the administration of local anesthesia, 88% of the carious teeth with MIH group and 100% of the carious teeth without MIH group were unresponsive to EPT, and the difference was nonsignificant ($p \geq 0.05$).

The results of intraoperative pain scores differed significantly between MIH presence or absence. Carious teeth in the MIH group had higher results ($p = 0.003$). Additionally, according to the records, none of the patients in the carious groups reported unbearable pain during the treatment procedures that would require the use of adjunct methods.

DISCUSSION

The present study was conducted with vital, asymptomatic permanent molar teeth free of caries and caries to standardize pulp status. Additionally, the groups were divided into subgroups as MIH and without MIH teeth as carious and caries-free teeth. The results showed a significant difference in anesthesia with sensitivity test assessments. Therefore, our first hypothesis was partly rejected, since no difference among the first EPT responses between carious teeth in the MIH group and carious teeth in the without MIH group was observed. Our second hypothesis was also partly rejected since no significant difference was present between the initial EPT scores of carious and caries-free teeth with MIH. However, the cold responses were found to be higher for carious teeth with MIH than for caries-free teeth with MIH.

It is expected that the presence of MIH results in a high susceptibility to dental caries development.[4,6,24] Findings from the present study also support that the ICDAS scores of the groups with MIH were significantly higher than those of the groups without MIH for carious teeth, even though there were no notable differences among the radiographical caries depth between the groups. These findings are similar to those showing that children with MIH have higher DMF (decay-missing-filled) scores for their first permanent molar teeth than children without MIH.[25,26] The high rate of caries

Table 2: First EPT and cold test results of the groups

Groups	1st EPT		1st Cold Test	
	n	mean ± sd	n	mean ± sd
Carious Teeth with MIH Group	25	4.9± 1.9^{A}	25	4.9± 2.5^{A}
Caries Free Teeth with MIH Group	10	5.1± 0.9^{A}	10	3.8± 2.3^{B}
Carious Teeth without MIH Group	25	4.8± 1.2^{A}	25	4.8± 1.5^{A}
Caries Free Teeth without MIH Group	10	5.9± 0.9^{A}	10	2.3± 0.9^{B}

Mann Whitney U Test, sd: Standard deviation, significancy level $p<0.05$. Superscript different uppercase letters withnin each colum shows statistical difference amongst groups.

Table 3: Comparison of first and second EPT and cold test results for carious teeth with MIH and without MIH

Groups	EPT				Cold Test			
	1st EPT		2nd EPT		1st Cold Test		2nd Cold Test	
	n	mean±sd	n	mean±sd	n	mean±sd	n	mean±sd
Carious Teeth with MIH Group	25	4.9±1.9^{A,a}	25	9.1±1.9^{A,b}	25	4.9±2.5^{A,a}	25	2.0±2.5^{A,b}
Carious Teeth without MIH Group	25	4.8±1.2^{A,a}	25	10.0±0.0^{A,b}	25	4.8±1.5^{A,a}	25	0.2±0.5^{B,b}

Wilcoxon Signed-Rank Test, sd: Standard deviation, significancy level $p<0.05$. Superscript uppercase letter within each column shows statistical difference amongst groups. Superscript lower case letters within each row for each test show statistical difference.

Table 4: Pain during the treatment scores for carious groups

	Groups n	Mann-Whitney U Test		
		mean±sd	p	
Pain during the treatment	**Carious Teeth with MIH Group**	25	1.9±2.52.5	**0.003**
	Carious Teeth without MIH Group	25	0.4±1.2	
	Total	50	1.2±2.1	

Mann Whitney U Test, sd: Standard deviation, significancy level $p<0.05$.

incidence for the MIH group can be caused by the hypomineralization of enamel combined with inadequate oral hygiene. Severely affected enamel subjected to masticatory forces soon breaks down, leading to unprotected dentine and rapid caries development. It is also known that the severity of MIH may increase caries incidence.[10,27] To standardize the study group as much as possible, only teeth showing typical caries with 3/4/5/6 ICDAS scores of asymptomatic teeth were enrolled in the carious MIH group. Although MIH molars with only post eruptive enamel breakdown are also in need of restoration, since they do not have any caries, they were not considered for the study population.

Although a precise explanation for hyperalgesia is lacking, apparently localized elevations in tissue pressure and inflammatory mediators that accompany acute inflammation play an important role.[28-31] Three characteristics of hyperalgesia are spontaneous pain, a decreased pain threshold, and an increased response to a painful stimulus. The peripheral mechanism for these symptoms includes a decrease in pain threshold level, an increase in responsiveness to noxious stimuli, and the development of spontaneous discharges of nociceptors. All three of these characteristics can be seen in patients experiencing inflammatory pain of pulpal origin.[32-34] According to the results of this study, caries was a more prominent factor than MIH for the initial cold results.

Dental caries and mineralization defects both might leave teeth vulnerable and induce pulp tissue to protect vitality. However, it is difficult to assess the certain state of the pulp without histological examination.[32,33,35,36] The results of the present study showed that the first EPT and cold test results were not significantly different between groups, suggesting that the initial state of dental pulp should not differ. On the other hand, when the responses for the second EPT and cold test for carious teeth with MIH and without MIH were evaluated, the results showed that hypomineralization affects the response of pulp tissue. Thus, even when teeth are anesthetized effectively, children with carious teeth along with MIH still feel pain.

The initial results for the cold test showed that caries affects the responses more predominantly than the presence of MIH, as mentioned above. However, the results also showed that while local anesthesia lowers the values of cold responses, it cannot eliminate them completely, and the presence of MIH makes the responses to the cold tests significantly more notable. The results of the present study suggest that hypomineralization significantly affected pulp tissue with a significant continuous response to cold, despite the administration of local anesthesia for carious teeth.

The other sensitivity method used in the present study was EPT. The working principle of EPT is to stimulate intact myelinated A-delta fibers within the pulp-dentine complex by applying electric current to the tooth surface. As a result of the ionic current of dentine fluid in the dentine ducts, the action potential of intact A-delta fibers is generated, and a positive result is obtained.[37,38] The present study showed that second EPT values for teeth without MIH were significantly higher than teeth with MIH for carious groups.

The difference between the first and second EPT or cold test values might be related to the pulp response after anesthesia. The response of EPT and cold test might be differentiated because of the mechanism of action against the A-delta fibers for carious teeth with MIH and without MIH. The results indicate that anesthetics had an inducement effect on carious teeth, which was due to the significantly higher second EPT values than first EPT values. The second cold test values were significantly lower than the first values, and this result might also be related to the effectiveness of anesthesia. Even though the cold responses were decreased after the administration of local anesthesia, they were not eliminated completely for carious teeth with MIH.

Rodd *et al*[7] demonstrated on extracted teeth that MIH challenges pulp when compared to teeth without MIH. It has been shown that hypomineralized permanent first molars demonstrate changes in pulpal innervation, vascularity, and immune cell accumulation that are indicative of underlying pulpal inflammation and may help to explain the heat sensitivity experienced by some patients. These studies[1,4,6,7] showed that even caries-free teeth with MIH might have pulpal inflammation. Although the present study did not investigate the histology of the pulp of carious teeth with MIH, the results suggested that when MIH teeth have caries, pulpal condition is much more affected since the initial EPT results and cold test showed that those teeth are significantly more sensitive than teeth without caries with MIH.

According to the results, there was a significant difference between the groups for carious teeth with MIH and without MIH for pain during the treatment procedure. The intraoperative pain was significantly higher for carious teeth in the MIH group. This result might also be related to the different pulp tissue structures. Hypomineralization might leave the tooth vulnerable to environmental factors, which is due to weak enamel and widened dentine tubules. Therefore, this enamel-dentine differentiation might cause high-level sensitivity of pulp tissues.[39,40]

Within the limitations of this study, these different EPT and cold test results might be correlated with hypomineralization. Thus, this study may add some evidence to the difficulties in anesthetizing teeth with MIH. EPT provides information about nerve conduction and the presence of nerve fibers, but the integrity and health status of the pulp cannot be determined. According to the literature, there was no correlation between the positive response of pulp tissue and the histological status of the pulp.[37] One of the limitations of the present study is that even though we attempted to standardize the characteristics of the carious lesions in enrolled teeth, one should keep in mind that it will never be possible to provide exact caries characteristics, such as radiographic caries depth and ICDAS scores, for all included teeth.

In the present study, block anesthesia for both maxillary and mandibular teeth was applied to ensure anesthesia effectiveness. Effectiveness of anesthesia controlled with the presence of numbness with a fine-tipped probe. The failure of anesthesia is generally controlled by numbness in the lip, cheek, and tongue, but these findings may not be as accurate as EPT. In the present study, the clinician performing the restoration was blinded to the EPT scores to mimic the clinical conditions, since EPT is not a routine application for controlling the effectiveness of anesthesia. Therefore, we relied on numbness, rather than EPT results, to confirm the presence of anesthesia. However, the results from the present study showed that 88% of the carious group with MIH and 88% of the group without MIH showed 100% unresponsive to EPT. The difference among the groups was not significantly different, suggesting that both groups were effectively anesthetized. Even though the patients

reported discomfort during the restoration, none of them reported it to be unbearable and required further intervention. It should be kept in mind that all the patients in the present study scored 4 or 5 anxiety level with the Modified Frankl Scale, which shows the highest compatibility, and the results might differ when the anxiety level of patients also differs.

Another suggestion for providing anesthesia is the use of analgesics before the administration of local anesthesia for teeth with irreversible pulpitis.[41,42] In addition, recent research has addressed the effectiveness of intraosseous anesthesia in MIH.[35,43] The use of ozone therapy, lasers and remineralizing agents with casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) has been effective in eliminating hypersensitivity in caries-free teeth with MIH for anterior teeth.[23] Since the findings from the present study showed that pulpal anesthesia is achieved but responses to cold tests for MIH teeth are not totally eliminated, preoperative administration of analgesics, drugs or the use of different remineralizing agents before the treatments might be helpful in reducing the sensitivity to cold. Detailed further studies are needed to confirm this finding.

CONCLUSIONS

Hypersensitivity in MIH teeth is an important issue that leads us to improve our treatment procedures, such as adding ozone therapy, CPP-ACP, analgesics, behavior management methods or sedation/general anesthesia, to provide more comfortable treatment sessions for patients. This prospective clinical study showed that the administration of local anesthesia before treatment provides sufficient anesthesia; however, it does not eliminate the feeling of cold and pain during treatment. Therefore, it might be concluded that supplemental or more local anesthesia would not be helpful to eliminate sensitivity; alternative methods should be investigated along with further histopathological studies to solve this hypersensitivity problem in MIH teeth.

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