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Review Article

Comparison of aesthetic treatments for molar-incisor hypomineralisation: Systematic review and meta-analysis

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ABSTRACT

Introduction: Molar incisor hypomineralisation (MIH) is a developmental defect that predominantly targets the first permanent molars and incisors and consists of hypomineralisation of the enamel. A range of treatment options are available to improve aesthetics in this condition, including resin infiltration, bleaching techniques, restorations, microabrasion, and laser therapy.

Objectives: This systematic review and meta-analysis aimed to analyse the effects of treatments on changes in enamel colour in teeth with MIH lesions and determine whether resin infiltration is the most aesthetic treatment.

Material and Methods: A systematic literature search was conducted on PubMed, Web of Science, EBSCO, and Scopus databases until December 2022. The addressed PICO question was: "Is resin Infiltration the most effective treatment for restoring aesthetics in comparison to other treatments in patients with Molar incisor hypomineralisation?''. In addition, a meta-analysis was conducted with the selected studies to integrate the information using R.51 software (R Core Team (2013)).

Results: In total, 678 articles were obtained from the initial search, of which 11 met the inclusion criteria. Seven studies concluded that resin infiltration was the most successful treatment method in the aesthetic rehabilitation of MIH lesions. Six of the eleven articles were included in the meta-analysis, which indicated that the treatments generated substantial colour changes.

Conclusions: This systematic review and meta-analysis provided significant data suggesting that resin infiltration is the most effective treatment for achieving aesthetic improvements in MIH lesions, with the meta-analysis providing a significant result ($p = 0.051$) in favour of the hypothesis.

1. Introduction

Molar incisor hypomineralisation (MIH) is a developmental defect that involves hypomineralisation of the enamel, most frequently targeting one or more of the first permanent molars and incisors (Bulanda et al., 2022). The prevalence worldwide is increasing, along with other associated dental complications among these patients (Almuallem and Busuttil-Naudi, 2018). The rising concern regarding this condition is owing to its impact on the quality of life of paediatric patients and the challenges faced with its clinical management. The resulting effect of this condition is increased sensitivity, predisposition, and rapid progression of caries and post-eruptive enamel breakdown, in addition to cosmetic and psychosocial issues, particularly when the anterior teeth are involved (Rodd et al., 2021). The affected dentition is considered to have a poor long-term prognosis because of diminished structural integrity and increased vulnerability to caries (Silva et al., 2016). The lesions are cream-white to yellow–brown in colour and are clearly demarcated, making it easy to distinguish between sound and affected enamel. Clinically, the enamel is soft, porous, and brittle, which can result in fragments that easily chip off under occlusal forces (Allazzam et al., 2014).

There are different treatments available aimed to address the aesthetic consequences of MIH, these include: bleaching technique, microabrasion, restorations (composites, metallic and zirconia crowns), laser treatment, and resin infiltration such as ICON® system (DMG, Hamburg, Germany).

Given that the information comparing the different treatments and providing conclusive data on which treatments are most effective for

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enhancing aesthetics is currently lacking, the aim of this systematic review and meta-analysis was to evaluate and determine the most effective aesthetic treatment for patients with MIH by addressing the following question: "Is resin infiltration the most effective treatment for restoring aesthetics in comparison to other treatments in patients with molar incisor hypomineralisation?''. In addition, through a meta-analysis, this information was intended to be integrated from different studies, thereby obtaining a general conclusion about the research object.

Hypothesis

H0: The hypothesis of this systematic review and meta-analysis was that the most effective treatment for achieving the best aesthetic outcome is resin infiltration.

H1: The null hypothesis was that resin infiltration is not the most effective treatment to achieve the best aesthetic outcome for MIH lesions.

Objectives

This systematic review and meta-analysis aimed to analyse the effects of treatments on changes in enamel colour in teeth with MIH lesions and determine whether resin infiltration is the most aesthetic treatment.

2. Materials and methods

Details on search methodology are as follows: we selected the database, outlined the search strategy, conducted screening and paper selection, and performed statistical analysis).

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Metal-Analyses (PRISMA) guide (Page et al., 2021). The following structure was used to formulate the review questions:

- P (Population): Patients with molar incisor hypomineralisation
- I (Intervention): Resin infiltration treatment
- C (Comparison): Bleaching technique, microabrasion, restorations, and laser treatment
- O (Outcomes): The best aesthetic treatments for molar incisor hypomineralisation

The PICO question: 'Is resin infiltration the most effective treatment for restoring aesthetics in comparison to other treatments in patients with molar incisor hypomineralisation?'.

2.1. Eligibility criteria

The selected studies adhered to the following inclusion criteria:

- **Type of study**: Randomised controlled clinical studies, systematic reviews, retrospective studies, and non-randomised controlled clinical studies; publications in English; articles published between January 2012 and December 2022.
- **Types of patients**: Hypomineralisation affecting the permanent first molars and permanent incisors.
- **Type of Intervention**: Treatment with microabrasion, whitening, restoration, laser, or resin infiltration.
- **Type of Outcome variables**: Studies that provided data on the aesthetic outcomes of treatments for both anterior and posterior teeth.

2.2. Search strategy and study selection

A comprehensive electronic search was conducted by one investigator (N.S.M.) using PubMed, Web of Science, EBSCO, and Scopus databases. The initial keywords used were as follows: 'hypomineralisation', 'hypomineralization', 'microabrasion,' 'whitening', 'bleaching', 'etch-bleach-seal', 'preformed metal crowns', 'stainless steel crowns', 'prefabricated crowns', 'veneers', 'indirect restorations', 'laser', 'resin infiltration'. These keywords were combined with Boolean operators 'AND' or 'OR' with an advanced search, in addition to the MeSH terms generated for PubMed, to obtain the most suitable and widest range of search results. The PubMed search filters included full texts and articles published within the last 10 years (between 2012 and 2022). The search strings used for the other databases were modified using the Polyglot Search Translator Tool (https://sraccelerator.com/#/polyglot) (40). A summary of the searches for each database is reported in Table 2, which is included in the Annexes. The final search was conducted on 20 December 2022. The same search was conducted by N.S.M. in February 2023 to check if new articles were published more recently; however, no new articles were found, and the number of search results remained consistent with the preliminary search.

The search in PubMed, Web of Science, EBSCO and Scopus was as follows: (((hypomineralisation AND whitening) OR (hypomineralisation AND bleaching) OR (hypomineralisation AND 'etch-bleach-seal')) OR ((hypomineralisation AND microabrasion)) OR ((hypomineralisation AND 'preformed metal crowns')) OR (hypomineralisation AND 'stainless steel crowns') OR (hypomineralisation AND 'prefabricated crowns') OR (hypomineralisation AND veneers) OR (hypomineralisation AND 'indirect restorations')) OR ((hypomineralisation AND laser)) OR (hypomineralisation AND 'resin infiltration'))). These searches were performed individually across the different databases to obtain relevant articles regarding each type of treatment used for MIH.

2.3. Selection process of studies

The studies obtained were filtered by title, abstract, and full text. The first stage involved reading the titles of the articles and eliminating those that did not meet the requirements of the selection criteria or those that were irrelevant based solely on the title. Any duplicates found across different databases were manually removed. Following this, in the second stage, the abstracts were read, whereby a summary of the objectives, methodology, conclusion, and discussion was read, and selection criteria were applied, resulting in the removal of articles that did not comply with the criteria. Finally, in the third stage, another round of screening was conducted, whereby the studies were filtered after reading the full texts and the required relevant data were extracted. Any studies that involved the survival rate of the restorations and those that used preventative measures as a primary treatment to compare with the indicated minimally invasive treatments were deemed irrelevant and were excluded. The articles were further screened by a supervisor to confirm their eligibility, and additional articles were removed if they were deemed irrelevant to the current review. Following discussion with Dr. S.M.R., all case reports, questionnaires/surveys, and literature reviews were excluded to obtain articles that were most relevant and consisted of information that had reduced bias. Any disagreements regarding selected studies were discussed and resolved by the reviewers. Using Cohen's kappa test, the degree of agreement between the selected studies from the second and third stages was calculated. Overall, two investigators (N.S.M. and S.M.R.) were involved in the selection process to determine the studies included.

2.4. Data extraction

A table was generated to highlight the relevant information. The categories within the table include the title of the article, authors, the year of publication, the sample size (if documented), the types of treatments included, any complications mentioned in the article, and the best treatment suggested by each article. For the meta-analysis, data extracted from the articles included the standard deviation, mean, and number of teeth involved in each study. This was administered both

prior to and after the treatment to analyse the effect of the treatment on aesthetics.

2.5. Data synthesis

To summarise and compare the different outcomes and variables across the different studies, a meta-analysis was conducted to evaluate the data obtained. The analysis was carried out to assess the effectiveness of treatments on aesthetics restoration of the teeth by comparing data obtained before and after treatment. The researchers conducted a comprehensive review of the literature, with a final number of studies totalling 11. Of the 11 studies, only six provided sufficient information for the development of a meta-analysis. The primary outcome of this study was colour change. Because the variables and units of measure-

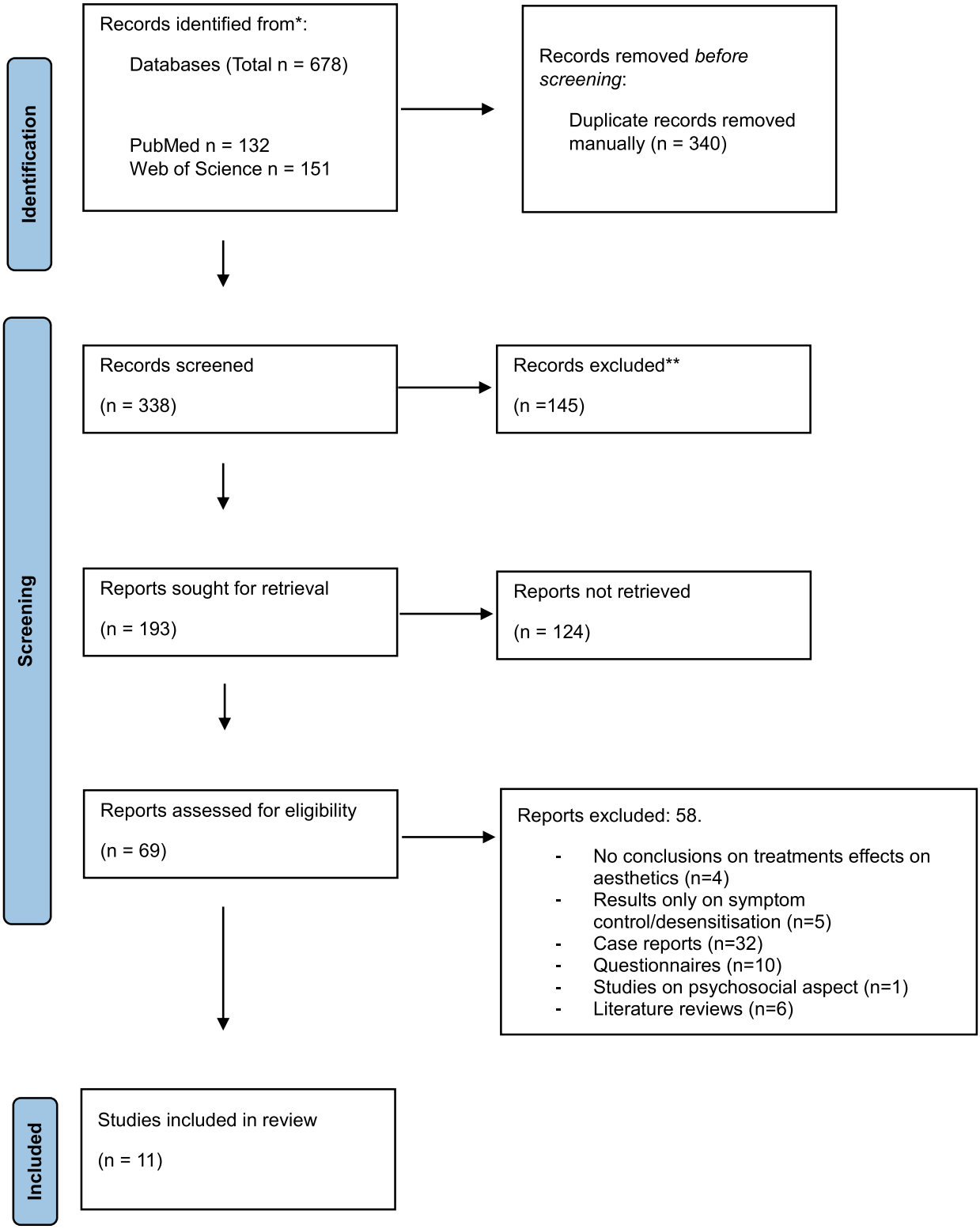

Fig. 1. The scheme followed in the selection of articles is based on the PRISMA Flow chart.

ment used in each study were not the same, considerable heterogeneity existed across the studies. In all the analysed studies, the Δ value, mean difference, or the visual analogue score (VAS) can be interpreted as a score of the magnitude of the colour change produced. Therefore, the statistical methodology used was based on the estimation of the standardised mean variation. For the meta-analysis, the magnitude of colour change specific to the treatment used was estimated, and the standardised mean change (SMC) was calculated with 95 % confidence intervals (CI) from random effects models with a maximum likelihood estimator. It is important to consider that both the Khanna and Mazur studies provided pre- and post treatment values with their respective means and standard deviations. Therefore, to incorporate these studies, a sensitivity analysis was required, whereby different estimates were made for different degrees of correlation (low, medium, and high); hence, three models were created. We calculated the heterogeneity index I^2 (percentage of variability that estimates the effect that can be attributed to the heterogeneity of the true effects) and the corresponding statistical test for null Q. It is assumed that this information will have certain limitations, as the different scales of measurement indicate that the variability found cannot be attributed to differences between studies. The results of the estimates, overall effect measures, and CI were plotted in a forest plot. Publication bias was evaluated using funnel plots and the Egger's test. The significance level used in the analyses was set at 5 % ($\alpha = 0.05$). The software used for the meta-analysis was R 3.5.1 (R Core Team (2013)). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

2.6. Quality and risk of bias assessment

The remaining five studies not included in the meta-analysis were analysed and compared based on a descriptive study of the variables. The risk of bias was evaluated to analyse the methodological quality of the included articles. The JADAD scale, Newcastle–Ottawa scale, and the PRISMA statement were used to assess randomised controlled trials, non-randomised studies, and the quality of systematic reviews, respectively.

3. Results

A total of 678 articles were obtained from the initial database search: PubMed (n = 132), Web of Science (n = 151), EBSCO (n = 222), and Scopus (n = 173). Prior to screening, 340 articles were manually removed as duplicates, leaving 338 articles to be screened. Of these publications, 193 were retrieved and considered potentially eligible after screening the title and abstract. Full texts were obtained, and the exclusion criteria were applied. Subsequently, 69 articles were obtained and evaluated in detail, and 58 articles were excluded from the review (exclusion criteria are presented in the flowchart; Fig. 1). As a result, 11 articles met the criteria for inclusion and were included in the systematic review. All data extracted from the included studies are presented in the results table. The k-value for inter-examiner agreement on the inclusion of studies was 0.96, indicating 'very good' agreement according to the Landis and Koch criteria.

This meta-analysis produced three models based on different degrees of correlation: low (Model 1), medium (Model 2), and high (Model 3). Because Khanna and Mazur provided pre- and post-measurements, they were compared according to different degrees of correlation. It is important to note the analysis was conducted by both including and excluding Gençer's article; this was necessary as the Gençer's article reported a significantly larger change value compared to the other articles, which, when included, resulted in a larger standardised change. All three models showed a significant variation in colour; however, as Model 2 (r = 0.5) showed a medium correlation, it was selected to demonstrate the results.

3.1. Model 2 (medium correlation)

For this model, the degree of correlation between the pre- and post-measures of the articles from Khanna and Mazur was assumed to be medium (r = 0.5) (Gençer and Kirzioğlu, 2019; Bhandari et al., 2019). Information on the final inputs of the meta-analysis is shown in Table 1. The forest graph was entirely conditioned by the results obtained from previous studies, and the estimated SMC values were unitless and dimensionless.

With respect to the meta-analysis, assuming that Gençer's article is included and using Model 2, there was a slight significance supporting the hypothesis that the procedure induced colour change.

In this case, the meta-analysis concluded an SMC of 3.27 (95 % CI: −0.02, 6.56), which contains zero by a very small margin. Therefore, a very strong non-significant trend (p = 0.051) was presented in favour of the hypothesis that the procedure has generated a colour change (shown in Table 2).

In this case, the estimations were made without including Gençer's article (Fig. 2).

The meta-analysis concluded an SMC of 1.62 (Table 3). The 95 % CI for this overall effect measure (1.07, 2.12) did not contain zero; hence, a significant variation in colour was observed (p < 0.001).

Here, the heterogeneity was high at 86.7 %, and the absence of publication bias was accepted, as shown in the Funnel plot (Fig. 2).

The meta-analysis results showed, that when Gençer's article was included, only a significant colour change (p = 0.041) was acceptable under the assumption of a strong correlation (Bhandari et al., 2018). Under the medium correlation model, the result was at the limit of significance (p = 0.051), and under the low correlation model, the trend was still very strong (p = 0.058). When Gençer's article was excluded, the variability between the studies decreased, which provided a significant result under any level of estimated correlation. Irrespective of the inclusion/exclusion of Gençer's study, the models indicated that the procedures and treatments were generating substantial colour changes.

4. Discussion

Through both meta-analysis and interpretation of the descriptive analysis of the included studies, information was integrated to determine the most effective aesthetic treatment. Across all 11 studies included in this systematic review, seven concluded that resin infiltration was the most successful in improving MIH lesions in terms of aesthetics. According to the meta-analysis, four of the six included studies concluded that the exclusive use of resin infiltration produced the best aesthetic outcomes when treating MIH lesions. For the meta-analysis, as explained previously, owing to the heterogeneity in the studies, both in terms of variables used and units of measurements, three models were produced based on different degrees of correlation (low, medium, and high). In addition to this, as Gençer's article obtained an even greater heterogenous result, the models were created by both including and excluding the data from Gençer's article. It is important to note that all articles included in the meta-analysis concluded that resin infiltration was the most effective treatment for masking MIH lesions. Furthermore, with Gençer's article being excluded, the between-study variability decreased and resulted in a much more significant outcome under any of

Table 1
Final input for the meta-analysis for model 2.

Author	ni	M1i	Sd1i	M2i	Sd2i	ri
Gençer et al., 2019	49	12.77	1.03	0	0	0
Bhandari et a.l, 2019	46	10.9	5.5	0	0	0
Khanna et al., 2022	51	78.385	9.242	71.706	9.167	0.5
Mazur et al., 2019	33	4.09	1.01	1.87	1.32	0.5
(Bhandari et al., 2018)	22	8.8	5.9	0	0	0
Hasmun, 2019	86	5.96	2.64	0	0	0

ni: number of cases; m: mean; sd: standard deviation

Table 2
Model 2 (including Gençer): Meta-analysis results for the magnitude of colour change, SMC, standard error (SE), 95% confidence interval, z-test (p-value), I-index^2 and Cochran's Q (p-value) for heterogeneity.

SMC	SE	IC 95 %	z (p-value)	I^2	Q_H (p-value)	Egger (p-value)
3.27	1.68	−0.02 6.56	0.051	99.6 %	<0.001***	<0.001***

*p < 0.05; **p < 0.01; ***p < 0.001.

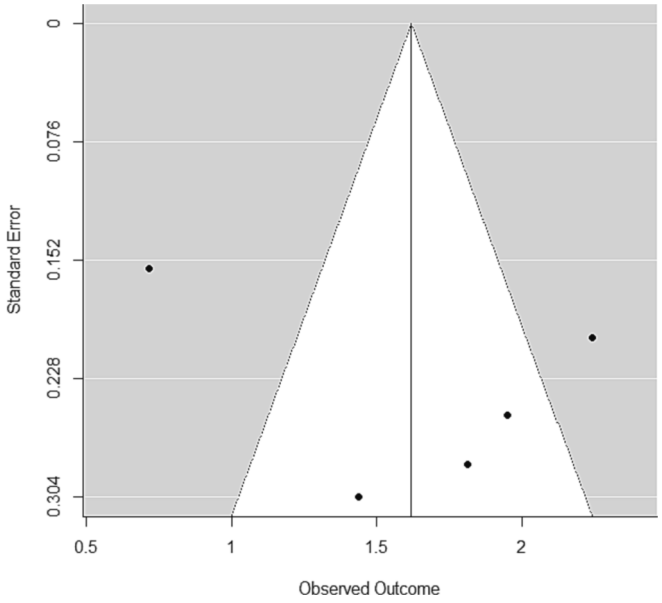

Fig. 2. Funnel plot excluding Gençer's article, for Model 2.

Table 3
Model 2 (excluding Gençer): Meta-analysis results for the magnitude of colour change, SMC, standard error (SE), 95% confidence interval, z-test (p-value), I-index^2 and Cochran's Q (p-value) for heterogeneity.

SMC	SE	IC 95 %	z (p-value)	I^2	Q_H (p-value)	Egger (p-value)
1.62	0.28	1.07 2.17	<0.001***	86.7 %	<0.001***	0.466

*p < 0.05; **p < 0.01; ***p < 0.001.

the estimated correlation models. Overall, according to the meta-analysis, under all the models generated, the treatments generated substantial colour changes, indicating that resin infiltration was the most effective treatment for aesthetics restoration/enhancement in patients with MIH.

Resin infiltration was most effective in masking mild lesions; however, for deeper lesions, alternative treatments may be required. Additionally, the results were case-dependent, and most studies highlighted the unpredictability of the aesthetic results obtained from resin infiltration.

The heterogeneity of the studies included in both the meta-analysis and descriptive analysis of this systematic review imposes a clear limitation on this systematic review, in addition to the bias presented in the studies. Many of the included studies focused exclusively on one type of treatment; therefore, the outcome was biased, as no other treatments were used for comparison. Within the meta-analysis, the variety in assessments and units of measurement made it challenging to produce a coherent conclusion that compared all articles in the same plane. However, this was combatted by creating several models of correlation to understand the pattern produced by the articles, which all showed that the treatments produced a colour change, despite the fact that it was to varying degrees.

The discrepancies in the assessment methods within the included studies revealed a mixture of quantitative (using a spectrophotometer) and qualitative (visual assessments) methods, thereby introducing another limitation. Furthermore, only two studies (Khanna et al., 2020; Mazur et al., 2018) provided data for pre-treatment and post-treatment, thus limiting the data produced in the meta-analysis.

Moreover, the methods used for analysing the results varied in the degree of reliability, with some studies using several observers to document the findings of the treatment to provide more reliable results, whereas other studies aimed to take repeat readings and obtain the mean to achieve more reliable results. Another factor to consider regarding quantitative measurements is the use of a spectrophotometer and the different conditions that were considered when taking the readings. The environment and location of the placement of the spectrophotometre on the lesion itself can impact the results obtained. Another limitation was the absence of a standardised protocol for conducting these measurements, which could have ensured consistency across the studies. Therefore, the heterogeneity in the methods of assessment in these studies highlights the need for further research and the formation of a protocol to facilitate a reliable and consistent assessment of such investigations and to enable better comparisons of the effectiveness of treatments for such lesions.

Finally, owing to the lack of studies on other treatments that were initially included in this systematic review, such as laser, bleaching, and restorative treatments, there was insufficient evidence to analyse the effects of such treatments on the aesthetic impact of MIH lesions. Therefore, future studies require a higher control of bias, and given the rising prevalence of MIH in children and adolescents, further research is required in this field to determine a more in-depth understanding of the effects of other treatments available for MIH and to obtain a detailed evaluation of the potential aesthetic improvements that other techniques can provi.

5. Conclusions

- The information on different treatments was integrated from a range of studies, providing a sufficient overview and conclusion on the aesthetic effectiveness of each treatment.
- Significant data suggested that resin infiltration is the most effective treatment for achieving aesthetic improvement in MIH lesions.
- The meta-analysis provided a significant result (p = 0.051) supporting the hypothesis that the procedure had induced a colour change.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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