Review Article

Esthetic Effects and Color Stability of Resin Infiltration on Demineralized Enamel Lesions: A Systematic Review

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ABSTRACT

Aims and Objectives: The aim of this study was to systematically review the ability of resin infiltration to conceal demineralized enamel lesions to normal enamel translucency and to maintain color stability. **Materials and Methods:** A literature search of PubMed, MEDLINE, Web of Science, and Scopus databases and a manual search of articles from 2009 to 2021 for randomized controlled trials (RCTs) and clinical efficacy trials (nonrandomized) were performed. Methodological quality and risk of bias (RoB) of included papers was assessed using Cochrane Collaboration Risk of Bias Tool 2.0 for RCTs and ROBINS-I (Risk Of Bias In Non-randomized Studies of Interventions) tool for nonrandomized studies. **Results:** A total of 352 titles and abstracts were reviewed. Eight RCTs and three clinical efficiency studies were included in this review. The masking effects of the demineralized enamel lesion were reported immediately after resin infiltration, and the color stability of this material was up to 24 months, with no adverse effects noted. For RCTs, four studies were classified as "some concerns" and four were as "low RoB." For nonrandomized studies, all of the studies presented an overall moderate RoB. **Conclusion:** Resin infiltration achieves the best esthetic outcomes compared with microabrasion and remineralization therapy. Color stability was achieved with this material for up to 24 months and no adverse effects were noted. Factors contributing to the esthetic outcomes of the resin include the elimination of the hypermineralized surface layer, the homogeneity of the resin itself, and polishing after resin infiltration. Longitudinal follow-up and improved control of confounding variables should characterize future high-quality systematic reviews.

Keywords: *Color stability, demineralized enamel lesions, esthetic, resin infiltration*

Introduction

Esthetics is a crucial aspect of dentistry.[1] Nowadays, with the development of materials and the high demand for maintaining the integrity of teeth, minimally invasive treatment has become a trend to maximize the esthetics of teeth.[1] This strategy is advantageous for the treatment of white spot lesions (WSLs) induced by demineralization and remineralization imbalances.[2] WSLs are an early indicator of demineralization beneath intact enamel, which occurs when pathogenic bacteria penetrate the enamel layer, resulting in the dissolution of calcium and phosphate by organic acids.[1,2] The decrease in mineral content beneath the intact enamel surface alters the typically translucent enamel light reflection, resulting in enamel opacity.[2,3] There have been reports of detrimental psychosocial effects, low self-esteem,

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and poor esthetics in children with WSLs on their anterior teeth.[1]

Remineralization is the first-line treatment for WSLs, such as fluoride therapy, casein phosphopeptide–based amorphous calcium phosphate pastes, or bioactive glass (calcium sodium phosphosilicate).[3,4] However, this therapy is dependent on patient compliance, and white lesions may persist despite strict dental hygiene and dietary counseling, thereby jeopardizing esthetics.[5] Therefore, resin infiltration was introduced to conceal the demineralized lesions and to preserve the natural translucency of the enamel.[6] Resin infiltration commercialized under the brand name ICON (DMG, Hamburg, Germany) is a novel technology that uses the concept of infiltrating the caries lesion with a low-viscosity resin to halt the progression of noncavitated caries lesions without requiring the removal of tooth structure.[6] In this technique, the tooth lesion surface is etched for 2 min with 15% hydrochloric acid; the tooth is then thoroughly dried, and finally, a low-viscosity resin is injected into the intercrystallite gaps of the demineralized enamel and the resin material is light cured.[6] Thus, the enamel pores that act as diffusion pathways for acids and dissolved minerals to reach the hypomineralized lesion are obstructed by the low-viscosity resin infiltrant.[6] In addition, due to the similar refractive index of the infiltrating resinous material as that of hydroxyapatite, the optical appearance of the affected enamel may bring it closer to the value of healthy enamel.[7] This is corroborated by a recent meta-analysis that revealed the superior camouflage effect of resin infiltration over remineralization therapy.[6-8] This approach fills, stabilizes, and reinforces demineralized enamel lesions without drilling tooth structure.[6,7] The aim of infiltrating WSLs with resin infiltration is to have highly esthetic results, not just immediately after the treatment but for a long term.[6]

Numerous thorough studies of the literature concluded that there are insufficient data to definitively support the use of resin infiltration in the treatment of WSLs on anterior teeth. This is due to a lack of high-quality clinical trials, not the technique of clinical inefficacy. The majority of available studies were laboratory based, had a high risk of bias (RoB), or were short term, making it difficult for the authors to make a definitive recommendation. Nevertheless, a meta-analysis conducted by Bourouni *et al.*[9] revealed a considerably greater optical improvement after infiltration compared to the routine application of fluoride varnish. The authors also stated that the concealing effects of fluoride varnish could take up to 6 months, as opposed to the immediate effect of resin infiltration.[9] A systematic review published in 2016 concluded that resin infiltration may be a viable option for color masking of WSLs and enamel development defects, but the authors called for additional research on this topic due to the small sample size and shorter follow-up time of the primary studies.[10] Following the publication of this systematic review, five new randomized controlled trials (RCTs)[11-15] and two new clinical efficiency studies[16,17] have been published. Given the recently published studies and the inconclusiveness of previous reports, we conducted an up-to-date, comprehensive systematic review to evaluate the esthetic effects of resin infiltration on demineralized enamel lesions and their color stability. This systematic review aimed to evaluate the efficacy of resin infiltration therapy in terms of esthetic appearance and long-term color stability of the results.

Research question

"Does resin infiltration camouflage demineralized enamel lesions to restore their normal enamel translucency and maintain their color stability?"

The study aimed to systematically review the ability of resin infiltration to conceal demineralized enamel lesions to normal enamel translucency and to maintain color stability.

The PICOS was explained as follows:[18]

1. Population (P): individuals of any age with demineralized lesions on WSLs in permanent teeth at baseline or after orthodontic WSLs;
2. Indicator (I): involvement of permanent teeth in WSLs;
3. Comparison (C): healthy adjacent enamel and other treatment modalities (microabrasion and fissure sealing);
4. Outcome (O): masking effects of resin infiltration on WSLs in permanent dentition, color stability, and adverse events of resin infiltration;
5. Study design (S): RCTs and clinical efficiency studies (nonrandomized).

Materials and Methods

Eligibility criteria

Eligible were both RCT and nonrandomized study designs that assessed the camouflage effect of resin infiltration on demineralized enamel. All English-language publications were accepted, with the exception of review articles, case reports, letters to the editor, expert opinions, meeting abstracts, unpublished articles, book chapters, dissertations, guidelines, and *in vitro* studies.

Search strategy

A detailed electronic search was performed in the following databases: PubMed, Science Direct, Web of Science, Scopus, and manual search. In each database, the search was performed using the text word and non-Medical Subject Heading (MeSH) to identify the descriptors. In addition, the Boolean search was performed in each database using the search terms "Resin infiltration" OR "ICON" OR "caries infiltration" AND "Esthetic" OR "Aesthetic" OR "Concealment" OR "Masking" OR "Camouflage" AND "Demineralized enamel lesions" OR "Early enamel lesions" OR "white spot lesions" OR "non-cavitated lesions" AND "color stability" AND "adverse effect" OR "complication."

Outcome assessment

The primary outcome was esthetics and secondary outcomes included color stability and the occurrence of adverse events.

Study selection and extraction

Studies were selected and articles were extracted using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[19] checklist in two phases. In the first phase, titles and abstracts were screened to identify preselected studies, whereas those that did not qualify were excluded. The full texts were retrieved if the titles/abstracts of the studies did not contain sufficient information to support a decision on inclusion or exclusion. In the second phase, the full texts of all included studies were assessed based on the same eligibility criteria. Data from each selected study were then extracted independently using a standard table that included the following: authors, year, study site, study design, age, number of subjects/gender, number of teeth, group, follow-up, type of lesion and debracketing time, protocol of resin infiltration, comparison, assessment, outcome, and conclusion.

Risk of bias in individual studies

The RoB for the RCTs was assessed through the Cochrane Collaboration Risk of Bias Tool 2.0.[20] On the basis of this RoB analysis, studies were classified under three categories: low RoB, some concerns, and high RoB. If at least one domain was rated as "some concerns" and all other domains as "low risk," the overall RoB could be rated as "some concerns." If several domains were rated as "some concerns," the overall RoB could be rated as either "some concerns" or "high," depending on the evaluation of the investigators. Consequently, if at least one domain was rated as "high RoB," the overall RoB had to be rated as "high."

For the nonrandomized studies, the Cochrane Collaboration ROBINS-I (Risk Of Bias In Nonrandomized Studies of Interventions) tool was used.[21] In this case, seven domains were considered: (1) bias due to confounding, (2) selection of participants, (3) classification of intervention, (4) deviations from intended intervention, (5) missing data, (6) measurements of outcome, and (7) selection of the reported result. The RoB was judged for each domain and resulted in an overall judgment of low RoB, moderate, serious, critical, or no information for each study. Likewise, the RoB assessment was performed by both reviewers independently and disagreements were resolved by consulting the third reviewer.

Results

Study selection

A total of 352 studies were identified during the electronic database search. After the removal of duplicates, 229 studies remained for consideration. Subsequently, 215 studies were excluded following the title and abstract screening, leaving 14 studies for consideration. In the end, 11 studies were eligible to be included in the review after the exclusion of studies that had no specific data needed for the review [Figure 1].

Study characteristics

Table 1 shows the characteristics of the included studies. All included articles were published between 2009 and July 2022. The total sample size was 236 participants (156 participants for the RCT and 80 participants for non-RCTs) with ages between 11 and 30 years and the mean age was 19.07 years. The total number of teeth involved was 1180, of which 1100 were from an RCT and 80 were from a non-RCT. Eight studies were RCTs[11-15,22-24] and three studies were non-RCTs/clinical efficiency,[16,17,25] all of these investigated the masking and color stability efficacy of resin infiltration on post-orthodontic except three studies related to natural WSLs.[16,17,23] Resin infiltration was compared with sound adjacent ena mel,[11,16,17,22-24] fissure sealant,[12] microabrasions,[14,15] remineralization pro and comprehensive care,[13] or mild or moderate demineralization.[25] Debracketing time prior to the resin infiltration application were from 1 week,[15,25] 3 months,[14] 1–12 months,[11,24] 5.1 months,[22] and 4 ± 2.5 months.[13] The follow-up period post-resin-infiltration varies among the studies selected up to immediately,[16] 1 week,[13,15,25] 8 weeks,[23] 6 months,[12,22] 12 months,[14,17,24] and 24 months.[11] Most of the studies followed the manufacturer's recommendation except Knösel *et al.*[22] and Knösel *et al.*[11] and Eckstein *et al.*,[24] in which hydrochloric acid was applied for about 6, 7, and 8 min and Senestraro *et al.*,[23] in which the WSLs

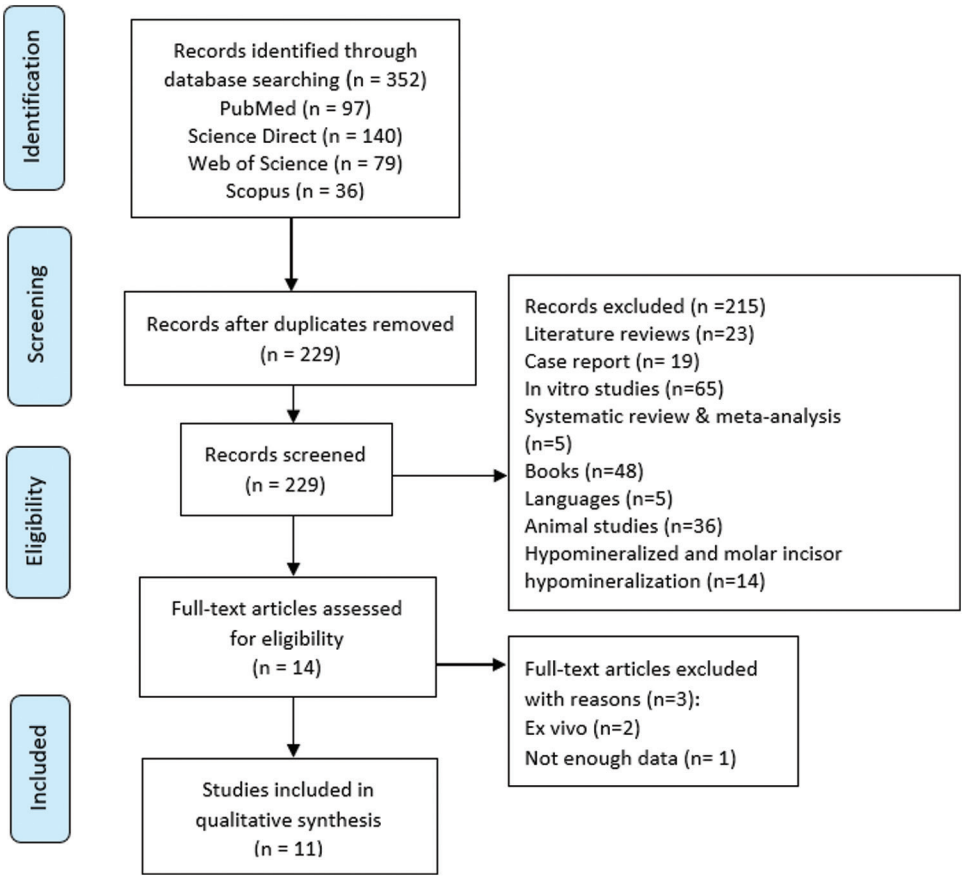

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

were abraded for 5 s by using a fine-grit polishing disk before application of resin infiltration.

Risk of bias within studies

The RoB assessment according to the RoB tools used in this review is described in Tables 2 and 3. Four RCTs were judged with some concerns about RoB due to randomization and missing outcome.[6,8,10,11] For nonrandomized studies, all of the studies presented an overall moderate RoB. The major problematic domains were as follows: bias due to confounding factors and the selection of participants for the study. However, the studies were judged as sound for nonrandomized trials considering this inherent study design limitation.

Discussion

This review was able to summarize the RCTs and clinical efficacy studies (nonrandomized) on the masking effects of resin infiltration in demineralized enamel lesions. It was found that resin infiltration is an effective method for achieving satisfactory effects in demineralized enamel lesions with a maximum follow-up period of 24 months.[11] Resin has a refractive index of 1.475, which is closest to the refractive index of enamel (1.65).[22] This reduces the difference in refractive indices between enamel porosities and healthy enamel, and the lesions regain their translucency and look similar to the surrounding enamel.[22,23]

Resin infiltration showed a significantly higher esthetic improvement of demineralized enamel lesions than microabrasion[14,15] and remineralization pro and comprehensive care.[13] Conversely, the esthetic effects of resin infiltration were found to be inferior when compared with fissure sealant after 3 and 6 months of follow-up, although immediate esthetic results were recorded for both resin infiltration and fissure sealant immediately after the application.[12] This is a result of bisphenol A-glycidyl methacrylate increased resin reactivity and reflectivity in fissure sealant, which immediately improves WSL esthetic characteristics.[12] Fluoride and calcium glycerophosphate from the glass matrix reservoir likely caused a slight increase in lightness over time, thereby enhancing the esthetic results.[13]

Most studies followed the manufacturer's protocol for the use of resin infiltration. Only in a few studies,[11,22,24] the etching time was modified and extended (6, 7, and 8 min) using the hydrochloric acid gel to achieve an optimal camouflage effect. Repeated etchings were

Table 1: Summarized data collected from the selected studies

Study/ Author/ Country	Study design	Age/ mean age/age range (year)	Number of subjects/ gender	Number of teeth/ group	Follow-up	Type of lesion/ debracketing time	Protocol of RI	Tools	Comparison	Mean ± SD/ *P* value	Result	Conclusion(s)
Hammad *et al.*[25] Egypt	Clinical efficiency	15.3	18/NA	18	Before infiltration (T0), Immediately (T1),7 days (T2)	Post orthodontic WSL RI was performed 1 week after debonding	Etch RI -2X Polish	Image J software	G1(mild demineralization) G2 (moderate demineralization)	G1 T1: Color masking of the WSLs =36%. T2: Total color masking of the WSLs =76%. G2 T1: Color masking of the WSLs =41%. T2: Total color masking of the WSLs = 63%.	Both groups had a statistically significant difference at $P < 0.05$.	The efficiency of the masking effect depends on the depth of the lesions, and the mild WSLs were masked better than the moderate lesions.
Knösel *et al.*[22] Germany	RCT	12–19	21 10(M) 11(F)	231 RI=111 C=108	Before infiltration (T0),1 day (T1), 1 week (T2), 4 weeks (T3), 3 months (T4), 6 months (T5)	Post orthodontic WSL RI was performed 5.1 months after debonding	Etch-6/7/8 min RI -2X Polish	Spectrophotometer	RI C(SAE)	RI - T0 vs T5 =2.55±4.24 P > 0.001* C - T0 vs T5 = 0.29±2.38 $P = 0.35$	No significant changes over 6 months.	RI improved the esthetic appearance of demineralized teeth and showed adequate durability for 6 months. No adverse events or side effects were observed.
Senestraro *et al.*[23] Portland	RCT	12–30	20/NA	66 46=RI 20=C	Before infiltration (T1), Immediately after RI (T2), 8 weeks (T3)	WSL	Abraded the WSL for five seconds by using a fine-grit polishing disk Etch-3X RI -2X Polish	Visual analog score & Image J software	RI C (SAE)	Mean VAS Reduction in WSL area -T2 RI=61.8% C=-3.3% $P < 0.001$ Reduction in WSL area -T3 RI=60.9% C=1% $P < 0.001$	The results showed no significant difference in percentage reduction between T2 and T3 in both the treatment and control groups.	The significant improvement compared to control teeth immediately after treatment. RI significantly improved the clinical appearance of WSL, with stable results eight weeks after treatment.

Table 1: Continued

Study/ Author/ Country	Study design	Age/ mean age/age range (year)	Number of subjects/ gender	Number of teeth/ group	Follow-up	Type of lesion/ debracketing time	Protocol of RI	Tools	Comparison	Mean ± SD/ *P* value	Result	Conclusion(s)
Eckstein *et al.*[24] Germany	RCT	13-19	21 10(M) 11(F)	231 117=RI 114=C	Before infiltration (T0), 6 months (T6), 1 year (T12)	Post orthodontic WSL Time elapsed following debracketing 1-12 months	Etch-6/7/8 min RI -2X Polish	Spectrophotometer	RI C(SAE)	Intergroup Comparison of Summarized ΔE Between WSL and SAE) between different assessments (T0, T6, T12) Time 1 (ΔE WSL/SAE) T0 T6 = 8.15 ± 3.74 Time 2 (ΔE WSL/SAE) T0 T6 = 6.33 ± 3.81 *P* < 0.001 Time 1 (ΔE WSL/SAE) T0 T12 = 8.15 ± 3.74 Time 2 (ΔE WSL/SAE) T0 T12 = 5.55 ± 2.61 *P* < 0.001 Time 1 (ΔE WSL/SAE) T6 T12 = 6.33 ± 3.81 Time 2 (ΔE WSL/SAE) T6 T12 = 5.55 ± 2.61 *P* = 0.08	Highly significant reduction of ΔE WSL/SAE discrepancies between T0 and T6, analysis of 12 months of records revealed color and lightness discrepancy of WSL vs SAE that was significantly decreased compared with baseline.	The color and brightness properties of RI, as well as the esthetic camouflage effects achieved by WSL infiltration, were not significantly or clinically relevantly altered after 12 months.

Table 1: Continued

Study/ Author/ Country	Study design	Age/ mean age/age range (year)	Number of subjects/ gender	Number of teeth/ group	Follow-up	Type of lesion/ debracketing time	Protocol of RI	Tools	Comparison	Mean ± SD/ *P* value	Result	Conclusion(s)
Knösel *et al.*[11] Germany	Split-mouth RCT	12-17	20 9(M) 11(F)	111	Before infiltration (T0), 6 months (T6), 12 months (T12), 24 months (T24)	Post orthodontic WSL Time elapsed following debracketing - 1 to 12 months	Etch-6/7/8 min RI -2X Polish	Spectrophotometer	RI C (SAE)	Intergroup ΔE WSL/ SAE Time 1 WSL SAE T0 T6 = 9.12 ± 5.63 Time 2 WSL SAE T0 T6 = 5.5 ± 2.76 *P* < 0.001 Time 1 WSL SAE T0 T12 = 8.58 ± 3.79 Time 2 WSL SAE T0 T12 = 5.2 ± 2.41 *P* = 0.01 Time 1 WSL SAE T0 T24 = 8.76 ± 5.34 Time 2 WSL SAE T0 T24 = 5.57 ± 2.62 *P* <0.001 Time 1 WSL SAE T6 T24 = 5.5 ± 2.76 Time 2 WSL SAE T6 T24 = 5.57 ± 2.62 *P* = 0.65 Time 1 WSL SAE T12 T24 = 5.2 ± 2.41 Time 2 WSL SAE T12 T24 = 5.57 ± 2.62 *P* = 0.35	Comparisons of T6, T12, and T24 with T0 yielded highly significant differences. A comparison of T6 and T12 with T24 revealed no significant differences.	Esthetic camouflage results obtained by infiltration of decalcified enamel are stable for at least 24 months. No adverse events or side effects were observed.

Table 1: Continued

Study/ Author/ Country	Study design	Age/ mean age/age range (year)	Number of subjects/ gender	Number of teeth/ group	Follow-up	Type of lesion/ debracketing time	Protocol of RI	Tools	Comparison	Mean ± SD/ *P* value	Result	Conclusion(s)
Kannan *et al.*[12] India	RCT	18 -20	12 7(M) 5(F)	193 teeth RI=102 Clinpro = 91	Before infiltration (T0), Immediately after RI (T1), 3 month (T2), 6 months (T3)	Post orthodontic WSL/NA	Etch RI Polish	Vita Easyshade Spectrophotometer	RI Clinpro	Intergroup and intragroup comparison of lightness values T0 RI = 73.60±7.71 Clinpro = 74.62±7.33 *P* = 0.295 T1 RI = 78.37±5.94 Clinpro = 78.93±5.40 *P* = 0.446 T2 RI = 80.08±6.46 Clinpro = 81.68±5.55 *P* = 0.041* T3 RI = 81.88±6.27 Clinpro = 83.69±5.29 *P* = 0.017*	Immediately after the intervention, RI showed statistically significant better improvement than Clinpro varnish in restoring the color however, at 3 and 6 months this was reversed.	Clinpro XT varnish showed significantly better improvement than RI in restoring the color and lightness of the WSLs at 3 and 6 months

Table 1: Continued

Study/ Author/ Country	Study design	Age/ mean age/age range (year)	Number of subjects/ gender	Number of teeth/ group	Follow-up	Type of lesion/ debracketing time	Protocol of RI	Tools	Comparison	Mean ± SD/ *P* value	Result	Conclusion(s)
Xi Gu *et al.*[14] China	Split-mouth RCT	12-19	20 8 (M) 12 (F)	128 T12-108	Before intervention (T0), 1 week (T1), 6 months (T6), 12 months (T12)	Post orthodontic WSL Debonding for more than 3 months	Etch-2/3 times RI -2x Polish-NA	Spectrophotometer	RI Microabrasion	Area ratio ΔE value T0 RI = 6.57 ± 2.48 Microabrasion = 5.62 ± 2.04 *P* = 0.1291 T1 RI = 2.21 ± 0.99 Microabrasion = 2.66 ± 1.02 *P* = 0.1034 T6 RI = 2.20 ± 0.82 Microabrasion = 2.26 ± 0.93 *P* = 0.7941 T12 RI = 2.03 ± 0.82 Microabrasion = 2.08 ± 1.06	In the RI group, the area ratio and ΔE had no significant changes over time from T1 to T12. In the microabrasion group, the area ratio and ΔE decreased significantly from T1 to T6.	RI and microabrasion improved the esthetic appearance of WSLs and showed adequate durability over 12 months. RI showed a better esthetic improvement effect after 12 months compared with microabrasion.
Andrade *et al.*[16] Brazil	Clinical efficiency	11-23	40 19(M) 21(F)	40	Immediately after	WSL	N/A	Spectrophotometer	RI SAE	Mean of the ΔE WSL vs SAE=8.05 ± 0.48 WSL vs RI=5.93 ± 0.41 RI vs SAE =5.77 ± 0.41 *P* < 0.005	The color of the WSL changed after treatment, but RI did not fully camouflage the WSLs when compared with the SAE.	RI treatment was not able to camouflage the color of the WSLs when compared with the SAE. However, RI is able to attenuate the color of demineralized enamel.
Giudice *et al.*[17] Italy	Clinical efficiency	12-29	2210(M) 12(F)	22	Before intervention (T0), Immediately after RI (T1), 1 year (T2)	WSL	Etch-1/2/3 times. RI -2x Polish	Spectrophotometer	RI SAE	ΔE (WSL vs SAE) at T0 vs T1: *P* < 0.01 (WSL vs SAE) at T1 vs T2: *P* = 0.935	The difference between ΔE (WSLs-SAE) at T0 and T1 resulted in statistical significance.	RI is immediately effective and the camouflage effect keeps up and steady one year after treatment.

Table 1: Continued

Study/ Author/ Country	Study design	Age/ mean age/age range (year)	Number of subjects/ gender	Number of teeth/ group	Follow-up	Type of lesion/ debracketing time	Protocol of RI	Tools	Comparison	Mean ± SD/ *P* value	Result	Conclusion(s)
Youssef *et al.*[13] Egypt	RCT	15 -30	15 7(M) 8(F)	45	1 week	Post-orthodontic WSL. Debonding 4 ± 2.5 months	Etch-1/2/3 times RI -2x Polish	Dell Technologies - CIE L*a*b* color system	RI RP CC	Difference in ΔE* RI = 11.29 ± 5.05 R*P* = 2.80 ± 0.84 CC = 0.88 ± 0.28 *P* < 0.001*	There is significant differences for RI vs RP (*P* = 0.029), RI vs CC (*P* < 0.001), and RP vs CC (*P* = 0.001).	RI is considered a temporally effective treatment option for the esthetic camouflage of WSL, whereas RP and CC failed to improve the appearance of the lesion in the short-term study. No significant adverse events or side effects were observed.
Shan *et al.*[15] Egypt	RCT	12-30	27	186	1 week	Post-orthodontic WSL. Debonding 1 week after	Etch-1/2/3 times	Image-Pro Plus	Microabrasion RI Control	Ratio WSL Microabrasion = 3.94 ± 0.03% RI = 45.02 ± 0.03% *P* = 0.96 >0.05 Control = 92.15 ± 0.02% *P* < 0.001)	ΔE (after to before) were similar between the control and the microabrasion. RI was significantly lower than those of the control and microabrasion group	RI and microabrasion are comparably effective in reducing WSL, but RI is more esthetic compared with microabrasion. No side effects were reported.

RI = resin infiltration, C = control, RP = remin pro, CC = complete care, WSLs = white spot lesions, SAE = sound adjacent enamel, N/A = not applicable, VAS = visual analog score

Table 2: Risk of bias of studies included in the qualitative synthesis based on the Cochrane Collaboration RoB 2.0 Tool

Study	Randomization	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Process selection of the reported result	Overall RoB judgment
Knösel *et al.*[22]	Low	Low	Low	Low	Low	Low
Senestrato *et al.*[23]	Low	Low	Some concerns	Low	Low	Some concerns
Eckstein *et al.*[24]	Low	Low	Low	Low	Low	Low
Knösel *et al.*[11]	Low	Low	Some concerns	Low	Low	Some concerns
Kannan *et al.*[12]	Low	Low	Low	Low	Low	Low
Xi Gu *et al.*[14]	Low	Low	Some concerns	Low	Low	Some concerns
Youssef *et al.*[13]	Some concerns	Low	Low	Low	Low	Some concerns
Shan *et al.*[15]	Low	Low	Low	Low	Low	Low

Table 3: Risk of bias of studies included in the qualitative synthesis based on ROBINS-I tools

Cochrane Collaboration Risk of Bias Tool for nonrandomized studies of intervention (ROBINS-I)								
Study	Pre-intervention		At Intervention		Post-intervention			Overall RoB judgment
	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended intervention	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	
Hammad *et al.*[25]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Andrade *et al.*[16]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Giudice *et al.*[17]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate

RoB = risk of bias

necessary and were dependent on the depth or degree of demineralization of the lesion in order to provide a preview of the anticipated esthetic outcome following infiltration.[11] In a study by Knösel *et al.*,[11] the frequency of etching was adjusted based on individual lesion depth as assessed by visual inspection. It has been shown that as the number of etching procedures or duration of etching increases, the esthetic result may improve due to increased resin permeability.[11] In addition, Kim *et al.*[26] showed a correlation between lesion depth and shade enhancement. Lesions deeper than the infiltration capacity of resin infiltration may show insufficient esthetic enhancement, according to the findings.[26] In deeper lesions, infiltration is more difficult because the pores are narrower and debris, saliva, organic material, and air may be present in the pores, making resin infiltration into the porous enamel more difficult.[27] This contradicts the findings of Ou *et al.*,[28] who investigated the impact of resin infiltration on enamel demineralization to varying degrees. The outcomes showed that both low- and high-enamel demineralization interventions had comparable concealing effects.[28] In all studies aimed at compensating for polymerization shrinkage, a dual application of resin infiltration was observed. This is in agreement with multiple studies and could explain why the disadvantages of the resins dissolved in ethanol were compensated when the infiltrants were applied twice to ensure complete obliteration of the lesion.[6-9]

Interestingly, in post-orthodontic WSLs, the time interval between bracket removal and resin infiltration seems to play an important role in the successful masking of WSLs. Consequently, the duration of debonding, which ranged from 1 week to 12 months in the included studies, will further optimize the esthetic results by remineralization with fluoride.[8,10,11,18-20] Although some may argue that waiting to treat white-spot lesions after bracket debonding allows for salivary tooth remineralization, a previous study recommended that resin infiltration application can be done as soon as possible after bracket removal to prevent further lesion progression that would result in surface integrity loss. In several studies, resin infiltration was applied 1 week to 1 year after debonding, and the esthetic results were promising with both methods (resin infiltration

immediately after bracket removal vs. resin infiltration after a period of remineralization).[8,10,11,18-20] It was reported that an increase in mineral volume from fluoride-assisted remineralization can significantly reduce the optical reflectivity of lesions within an enlarged surface zone.[23] Following the remineralization concept, the long-term stabilization of resin color was also influenced by the buffering capacity and flow rate of saliva, the individual's lifestyle, oral hygiene status, diet, and smoking.[19,20]

For the color assessment, qualitative analyses are less precise because they depend on the operator and are subject to variability associated with different observations over time.[24] In contrast, quantitative analysis using a spectrophotometer is considered the best evaluation tool for measuring tooth color changes (ΔE), as it provides excellent objective color assessment and provides accurate data.[26] On the basis of this quantitative measurement, each color is described in the CIE $L^*a^*b^*$ color system. It expresses color in three values: L^* for perceived brightness and a^* and b^* for the four unique colors of human vision: red, green, blue, and yellow.[19] A value of $\Delta E < 3.7$ is considered a clinically acceptable color difference.[19] In this study, the ΔE value after resin infiltration treatment among 6 months, 12 months,[19,20] and 24 months[11] did not prove to be statistically significant or clinically relevant. That is, the demineralized camouflage effects obtained by resin infiltration were found to be color stable and without significant changes over time.[19,20] It has been reported that the color stabilization after resin infiltration is due to the perfusion of the resin, which completely seals the cavity in the enamel.[24]

The follow-up period of 1 week to 24 months appeared to be quite short compared with the recommended 3-year follow-up for direct restoration and the recommended 5-year follow-up for indirect restoration.[29] Therefore, a long-term evaluation of clinical studies is needed in the future to assess the durability and longevity of the esthetic results of resin infiltration. The stability of the resin infiltration is affected by technical errors (improper handling of the resin), incomplete evaporation of the solvent, and loss of the oxygen inhibition layer.[29,30] In addition, the composition of the resin infiltrant, where triethylene glycol dimethacrylate (TEGDMA) is a highly hydrophilic monomer that is less resistant to degeneration in the oral environment, may contribute to color instability, which has been linked to the pigmentation tendency of TEGDMA due to the water carrier effect for various pigments.[30,31] The effects of pigmentation can also be affected by the duration of exposure and the intensity of coloring.[30] According to a recent systematic review, there have been reports of significant pigment changes following immersion in coffee, tea, red wine, and grape juice.[30]

In addition, a rough surface is considered a contributing factor to discoloration as it increases colonization by biofilms, which further promotes enamel demineralization and dissolution of the resin structure.[24] In all studies, the infiltrated resin was polished to reduce the surface porosity and remove the oxygen inhibition layer.[11,22,24,30] Polishing has resulted in a significant decrease in ΔE values because dyes are absorbed on the surface with low penetration into resin materials or the dental substrate.[30] Thus, the polished infiltrated lesions showed less discoloration than the unpolished infiltrated lesions.[11,22,24]

Regarding adverse effects, only three studies reported no local or systemic adverse effects of resin infiltration application during the 1-week to 24-month period.[8,10,20] In the included studies, no pain, loss of vitality, or discoloration were observed, indicating the safety of resin infiltration materials.[11,22,24,30] This is corroborated by a meta-analysis that found the absence of adverse events that confirmed the safety of microinvasive lesion management via resin infiltration.[32]

A limitation of this study was the lack of *in vivo* studies and the short follow-up period. Therefore, high-profile long-term clinical studies are needed to confirm the viability of resin infiltration in non-caries teeth. Variability among studies and heterogeneity in various parameters, including the time interval considered and the methodologies for evaluating esthetic and color stability, were limitations of this systematic review. Another limitation is that there is a lack of long-term studies on color stability and the study did not examine the esthetic effects of resin infiltration on other dental anomalies such as molar incisor hypomineralization, fluorosis, and amelogenesis imperfecta. Numerous parameters that influence camouflage effects, such as extension, depth, and activity of demineralized lesions, are, however, poorly addressed in the included systematic reviews. In the future, it will be necessary to conduct more high-quality clinical trials with long-term follow-up.

Conclusion

Resin infiltration is a beneficial technique for improving the esthetics of the demineralized enamel lesion to achieve the best clinical outcome compared to microabrasion and remineralization therapy. Color stability was achieved for up to 24 months with these materials and no adverse effects were observed clinically. The factors contributing to resin concealment

were the removal of hypermineralized surface layers, the homogeneity of the resin itself, and polishing after resin infiltration. Longitudinal follow-up and improved control of confounding variables should characterize future high-quality systematic reviews.

Recommendations for future research

Additional long-term RCTs on developmental enamel defects and long-term color stability evaluations, as well as an evaluation of the risk of discoloration or pigmentation are required to ensure the efficacy of the resin infiltration treatment.

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Conflicts of interest

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Authors contributions

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