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Review article

Is resin infiltration an effective esthetic treatment for enamel development defects and white spot lesions? A systematic review

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ABSTRACT

Objectives: To determine if resin infiltration is an effective treatment for improving the esthetic appearance of tooth discoloration resulting from development defects of enamel (EDD) and white spot lesions (WSL) by means of a systematic review.
Data sources: A comprehensive search was performed in PubMed, Scopus, Web of Science, LILACS, BBO Library, Cochrane Library, and SIGLE, as well as in the abstracts of IADR conference, and in the clinical trials registry.
Study selection: Clinical studies in patients with whitish tooth discoloration, in which the resin infiltration technique was applied, were included. Color masking was the primary outcome. The methodological quality and risk of biases of included papers was assessed using MINORS criteria for non-randomized (NRS) comparative studies and Cochrane Collaboration for randomized clinical trials (RCT).
Results: From a total of 2930 articles, 17 were assessed for eligibility and 11 remained in the qualitative synthesis. Four NRS and seven RCT studies were selected, the latter consisting of four full-text studies and three conference abstracts. Two studies were excluded from the quality assessment, due to overlapping results. The number of participants (treated teeth) ranged from 18 to 21 (38–74) in the NRS, and 20–83 (20–231) in the RCT studies. Post-orthodontic WSL were the most frequent treated lesions. Initial condition was used as control in the NR studies. In the RCT, resin infiltration was compared to non treatment, remineralization, or bleaching. Overall, partial or complete color masking of affected teeth was reported immediately after resin infiltration. Only two studies followed original outcomes up to one year and reported maintenance of original color masking. Two NR studies were assessed as “moderate” and one as “high” quality. Two RCT were classified as “low” risk of bias in the chosen key domains. The remaining four studies were considered “unclear” or “high” risk of bias.
Conclusion: Although the partial or total masking effect of enamel whitish discoloration has been shown with resin infiltration, there is no strong evidence to support this technique based on the present clinical studies.
Clinical significance: Enamel whitish discolorations in esthetically compromised areas are clinically undesirable. Minimally invasive approaches used as attempts to minimize the discoloration include the resin infiltration technique. The evidence for clinical recommendation of this technique is not strong, thus, further RCT studies with long-term follow-ups should be conducted.

1. Introduction

Whitish enamel discolorations can occur as a consequence of pre- or post-eruptive damage. Fluorosis, traumatic hypocalcification and molar-incisive hypomineralization (MIH) are conditions caused by disturbances during enamel development. The post-eruptive discoloration resulting from caries are called white spot lesions (WSL). All these conditions are associated with a reduction of the

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enamel mineral phase, altering its chemical composition and, consequently, its optical characteristics [1,2].

When these discolorations occur in anterior teeth, compromising the esthetical appearance, minimally invasive color-masking treatments can be used. Topical application of remineralizing agents [3,4], microabrasion [3], and bleaching [5] represent attempts to reverse enamel demineralization and/or to improve tooth appearance. The resin infiltration technique was also found to be useful in these cases [6].

Resin infiltration is based on the hydrochloric acid erosion of the lesion surface and posterior infiltration of a low-viscosity resin into the intercristaline spaces of hypocalcified or demineralized enamel. This alters the refractive index (RI) of the porous enamel, formerly filled with air (RI = 1.00) or water (RI = 1.33), since the infiltrated resinous material shows a RI (1.52) closer to hydroxyapatite (1.62). As a consequence, the optical characteristics of the affected enamel are altered and it seems like the surrounding sound enamel [7].

The penetration of the low-viscosity resin into porous enamel with caries or hypomineralization has been shown in *in vitro* studies. [8–10] Additionally, color masking efficacy with resin infiltration has been demonstrated using artificial caries models [7,11,12]. Some clinical reports also showed favorable esthetic results [2,6,13]. Nevertheless, there is a lack of evidence concerning the clinical efficacy of the technique for camouflaging enamel whitish discolorations.

The present study reports the findings of a systematic review focused on the following question: is resin infiltration an effective esthetic treatment for discolorations resulting from enamel development defects and/or white spot lesions?

2. Materials and methods

2.1. Protocol and registration

The study protocol was registered at the PROSPERO database (www.crd.york.ac.uk/PROSPERO) under the number CRD42015023862. The recommendations of the PRISMA statement for the report of this systematic review were followed [14].

2.2. Eligibility criteria

The search strategy was defined based on the elements of the PICO question:

Population: patients with enamel presenting color alterations arising from developmental defects (hypocalcification, hypoplasia, fluorosis, and hypoplasic molar-incisive syndrome) or white spot lesions, with no age restrictions.

Intervention: resin infiltration technique treatment.

Comparison: initial condition, no treatment or any minimally invasive treatment that aims to mask the discolorations (remineralization, bleaching, and microabrasion).

Outcome: esthetical results in terms of color masking.

Non-randomized study designs (before and after clinical condition comparison) and randomized clinical trials (RCT) that evaluated the masking effect of discolored enamel using resin infiltration were eligible. *In vitro* or *in situ* studies, editorial letters, pilot studies, historical reviews, case reports, and case series were excluded. When overlapping outcomes were identified, both the studies were included for data extraction, but only the study with the most complete data was assessed for risk of bias.

2.3. Sources and search strategy

An electronic search was performed in MEDLINE via PubMed (Table 1), Scopus, Web of Science, Latin American and Caribbean Health Sciences Literature database (LILACS), Brazilian Library in Dentistry (BBO), and Cochrane Library. An expert librarian (D.M.) supervised the search strategy. No restrictions were placed on the publication date or languages.

The grey literature was consulted using the database System for Information on Grey literature in Europe (SIGLE). The abstracts of International Association for Dental Research (IADR) were consulted (1990–2015) and authors from relevant studies were contacted for additional information. The registered clinical trials site (clinicaltrials.gov) was also accessed. Dissertations and theses were searched using the ProQuest Dissertations and Theses Fulltext database as well as the Periodicos Capes Theses database.

2.4. Study selection and data collection

The studies were initially selected by title and abstracts according to the previously described search strategy. Full texts were obtained for articles identified and judged as potentially eligible. The following data were extracted by two independent authors (A.B.B. and T.M.F.C) and recorded for each included study: study design, age of subjects, number of participants, number of treated teeth, type of lesion, type of treatment, outcome report, follow-up time, and final outcome details. The authors were contacted when data not described in the articles were necessary.

2.5. Risk of bias

Two independent reviewers (A.B.B. and T.M.F.C.) performed quality assessments of the included studies. The evaluation of non-randomized studies was based on a methodological index for non-randomized studies (MINORS) [15]. The MINORS items were classified as: 0- non-reported; 1- reported, but inadequate; 2- reported and adequate. The MINORS scale includes 12 items, the first eight being specifically for non-randomized studies. Since this tool was used only for non-randomized studies, with no distinct comparative groups, only the first eight items were considered. Scores were considered as: 0–4 “very low quality”, 5–8 “low quality”, 9–12 “moderate quality”, and 13–16 “high quality” [16].

Randomized clinical trials were assessed according to Cochrane Collaboration’s Risk of Bias tool. The criteria for judging risk of bias

Table 1
Method search (18/Feb/2016).

PubMed Search Strategy
(((((((((((((((((((((((((Dental Enamel[MeSH Terms]) OR Dental Enamel[Title/Abstract]) OR Enamel[Title/Abstract]) OR Fluorosis, Dental[MeSH Terms]) OR Dental Fluorosis[Title/Abstract]) OR Enamel Fluorosis[Title/Abstract]) OR Dental Enamel Hypoplasia[MeSH Terms]) OR Enamel Hypoplasia*[Title/Abstract]) OR MIH[Title/Abstract]) OR Amelogenesis Imperfecta[MeSH Terms]) OR Amelogenesis Imperfecta[Title/Abstract]) OR Tooth Calcification[MeSH Terms]) OR Enamel Defect*[Title/Abstract]) OR Enamel Maturation[Title/Abstract]) OR Tooth Discoloration[MeSH Terms]) OR Tooth Discoloration*[Title/Abstract]) OR Enamel Stain[Title/Abstract]) OR Teeth Discolorations[Title/Abstract]) OR Discoloration* Defect*[Title/Abstract]) OR Dental Caries[MeSH Terms]) OR Dental Caries[Title/Abstract]) OR Dental Decay [Title/Abstract]) OR White Spot*[Title/Abstract]) OR WSL*[Title/Abstract]) OR Tooth Demineralization[MeSH Terms]) OR Enamel Demineralization[Title/Abstract])) AND (((((Resins, Synthetic[MeSH Terms]) OR Synthetic Resin*[Title/Abstract]) OR Dental Resin*[Title/Abstract]) OR Resin infiltration[Title/Abstract]) OR Low viscosity resin[Title/Abstract])

a

Table 2
Data extraction from selected studies.

Study ID	Study Design	Subjects' age mean ± SD [range] (yrs)	Number of subjects (% male)	Number of teeth	Type of Lesion	Treatment	Outcome Report (parameter analyzed)	Follow-up time	Final Outcome
Kim et al. 2011 [23]	Clinical Efficacy (non-randomized)	12.5 (DDE) 15.1 (WSL/PO) [n.r.]	21 (n.r.)	38	DDE (MIH and hypocalcification) and WSL/PO	Resin Infiltration	Digital camera/image processing software (CIE $L^*a^*b^*$)	1w	% color changes: Completely masked (DDE = 25%, WSL/PO = 61%) Partially masked (DDE = 35%, WSL/PO = 33%) Unchanged (DDE = 40%, WSL/PO = 6%) Significant differences ($p < 0.05$) before and after treatment
Hammad et al. 2012 [24]	Clinical Efficacy (non-randomized)	15.3(1.7) [n.r.]	18 (n.r.)	n.r.	WSL/PO1 Without surface disruption WSL/PO2 With roughened surface	Resin Infiltration	Digital camera/image processing software (Histograms of gray scale from 0 to 225)	Immediate	WSL/PO1 Before = 126.09 After = 221.26 WSL/PO2 Before = 95.58 After = 155.61 Significant differences ($p < 0.05$) for both groups before and after treatment
Feng et al. 2013[a] [25]	Clinical efficacy (non-randomized)	n.r. [14–28]	20	74	WSL/PO	Resin Infiltration	Digital camera/image processing software (Histograms of gray scale from 0 to 225)	1w	% color changes: Completely masked 27% Partially masked 73% Unchanged 0 Significant differences ($p < 0.05$) before and after treatment (1w)
Feng & Chu 2013[a] [26]	Clinical efficacy (non-randomized)	n.r. [14–18]	8 (n.r.)	48	WSL/PO	Resin Infiltration	Digital camera/image processing software (Histograms of gray scale from 0 to 225)	1y	% color changes: Completely masked 22.9% Partially masked 77.1% Unchanged 0 Significant differences ($p < 0.05$) before and after treatment (1y)
Banava & Safaie Yazdi 2011 [31]	RCT	n.r. [n.r.]	n.r.	20	DDE (Fluorosis)	No treatment × resin infiltration	Visual analysis of photographs (Visual analog scale – VAS)	Immediate	Numerical data (n.r.) Significant differences ($p < 0.05$) between the groups
Wang et al. 2013 [27]	RCT	15 (n.r.) [12–27]	29 (48.27)	70	WSL/PO	Resin infiltration (RI) × remineralization (fluoride varnish- F)	Intraoral photo/visual analysis performed by dentists (reduction of the white affected area: 0% no reduction; 50% reduction of the half area, 100% complete masking)	6 m	RI = 53.5 x F = 49.2 Significant differences ($p < 0.05$) for both groups after treatment.
Knösel et al. 2013[b] [28]	RCT	15.5(n.r.) [12–19]	21 (47.61)	231	WSL/PO	Control (no treatment) × Resin infiltration (RI)	Spectrophotometer (CIE $L^*a^*b^*$)	6 m	ΔE baseline vs 6 months (RI = 2.55 × Control = 0.29). Significant differences ($p < 0.05$) between the groups
Senestraro et al. 2013 [29]	RCT	16.6 (1.8) [14–21]	20 (n.r.)	66	WSL/PO	Control (no treatment) × Short abrasion + Resin infiltration (RI)	Digital camera/Visual analysis (Visual analog scale – VAS: 0 = no change; 100 = complete masking and area measurement in square mm).	8 w	VAS (RI = 65.9 x Control = 5.7) Area reduction (RI = 60.9% × Control = 1%). Significant differences ($p < 0.05$) between the groups
Haddad et al. 2014 [32]	RCT	n.r.	83 (57.83)	n.r.	WSL/PO	Remineralization (Dentifrice with 5000 ppm F + Novamin) × resin infiltration	Laser fluorescence and visual analysis (Gorelick index)	3 m	Numerical data (n.r.) Significant decrease in the severity of WSL for both treatments ($p < 0.05$).
Eckstein et al.,	RCT	n.r. (n.r.) [13–19]	9 (55.5)	49	WSL/PO		Spectrophotometer (CIE $L^*a^*b^*$)	12 m	

Table 2 (*Continued*)

Study ID	Study Design	Subjects' age mean ± SD [range] (yrs)	Number of subjects (% male)	Number of teeth	Type of Lesion	Treatment	Outcome Report (parameter analyzed)	Follow-up time	Final Outcome
2015[b] [30]						Control (no treatment) × Resin infiltration (RI)			Significant differences achieved by infiltration after 6 months persisted after 12 months ($p < 0.05$).
Gugnani et al 2015 [33]	RCT	[6–14]	48 (n.r.)	80	DDE (Fluorosis)	Bleaching (B) × Resin infiltration (RI) × 2 applications RI (2RI) × BI + RI	Digital camera/image processing software (CIE L*a*b*)	6 m	ΔE baseline vs post-operative (2RI = 6.08 × B + RI = 5.95 × RI = 5.53 × B = 2.53). Significant differences: RI and 2RI > B ($p = 0.01$). No differences RI = 2RI = B + RI ($p > 0.05$). No significant differences for post-operative and after 6 m results.

n.r.- non reported.
DDE- Developmental defect of enamel.
WSL/POD- White spot lesion/post-orthodontic.
MIH- molar incisive hypomineralization.
[a] Same population study, with different follow-up times.
[b] Same population study, with different follow-up times.

covers six domains: selection bias (sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other sources of bias [17]. These domains were assessed at the study level. The risk of bias of each domain was classified following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 (http://handbook.cochrane.org). Since it was not possible to blind participants and personnel due to the nature of intervention, and no other source of bias was assessed, these two sources of bias were not included in the assessment method. The items random sequence generation, blinding of outcome assessment, and selective reporting were considered the key domains for the assessment of the risk of bias. The studies were classified as having a "low", "high", or "unclear" risk of bias [17].

2.6. Meta-analysis

As shown in Table 2, the selected studies showed a large variability due to different evaluation methods, such as spectrophotometry, digital camera combined with software analysis, and visual scale analysis. Thus, the outcome data were not comparable, since some studies presented CIE L*a*b* data, others exhibited histograms of gray scale, or percentage of reduction of white affected area. Additionally, the control groups in RCT studies also varied, with no treatment, fluoride varnish or dentifrice (remineralization), and bleaching used as the control. Therefore, a meta-analysis was not performed. Nonetheless, a comprehensive extraction of the study data was presented.

3. Results

3.1. Study selection

The search in the databases led to 3121 articles (Fig. 1). An additional three records were found in the IADR abstracts search. After the removal of duplicates, 2930 results remained. By title and abstract screening, the articles not related to the topic of this systematic review were excluded. Thus, 17 articles were assessed to verify if they were eligible. Among them, six were excluded due to the following reasons: case reports [6,18,19] and case series [20–22].

3.2. Study characteristics

The characteristics of the selected studies are listed in Table 2. The first four studies are non-randomized clinical efficacy design studies [23–26]. The following studies are RCT, consisting of four full-text studies [27–30] and three conference abstracts [31–33]. The studies from Feng & Chu [26] and Eckstein et al. [30] refer to the same sample as Feng et al. [25] and Knösel et al. [28], respectively, with long-term follow-up periods. Therefore, they were only considered for follow-up discussions and not included in the quality assessment.

The number of participants ranged from 18 to 21, with 38 to 74 treated teeth in the non-randomized studies, and from 20 to 83, with 20 to 231 treated teeth in the RCT studies. The focused population was young patients, with the age ranging from about 6 to 27 years old. The type of lesions treated was distinct. For the most part, in the studies post-orthodontic white spot lesions (WSL/PO) were treated [23–25,27–29,32], and in three of them, lesions were related to development defect of enamel (DDE) [23,31,33].

Regarding the final outcome, although a great clinical and methodological diversity was observed, partial or complete color masking was overall obtained using the resin infiltration

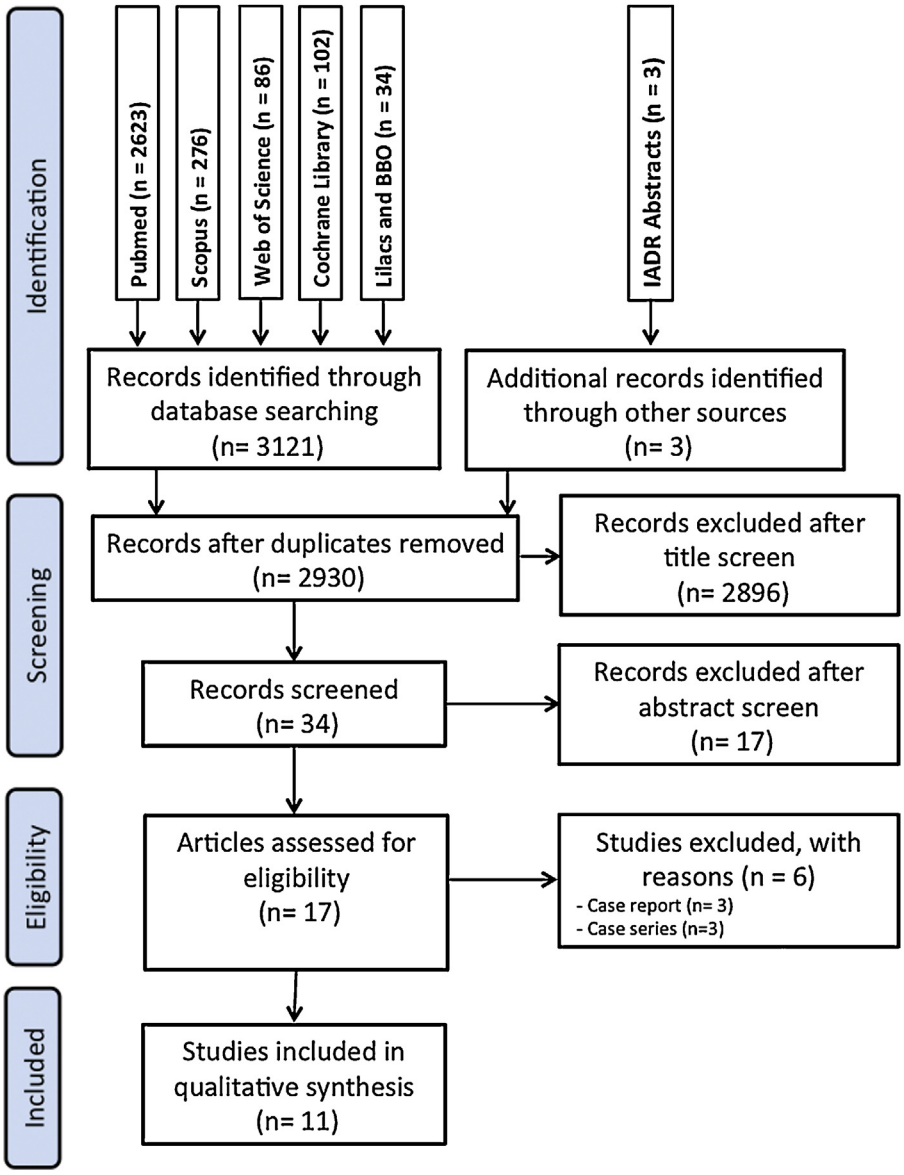

Fig. 1. Flow diagram of the study.

Table 3
Methodological appraisal of the selected studies according to MINORS assessment tool.

	Kim et al., 2011[a]	Hammad et al., 2012	Feng et al., 2013
Clearly stated aim	2	2	2
Inclusion of consecutive patients	2	0	0
Prospective collection of data	2	2	2
Endpoints appropriate to the aim of the study	2	2	2
Unbiased assessment of the study endpoint	2	0	2
Follow-up period appropriate to the aim of the study	2	2	2
Loss to follow up less than 5%	2	2	2
Prospective calculation of the study size	0	0	2
Total	14	10	12

2 = reported and adequate; 1 = reported but inadequate; 0 = non reported.
[a] authors provided extra information by e-mail to allow assessment of the risk of bias.

technique, with some differences in numerical results. When compared to the initial clinical situation (non-randomized studies), all studies reported significant differences before and after treatment [23–25]. The total masking effect for DDE and WSL/PO was reported as 25%/61%, respectively, and partial masking as 35%/33%, respectively, based on the CIE L*a*b* method [23]. In a

Table 4
Summary of the risk of bias for RCT studies according to the Cochrane Collaboration tool for assessing risk of bias.

	Banava & Yazdi 2011	Wang et al., 2013	Knösel et al., 2013	Senestraro et al., 2013	Haddad et al., 2014	Gugnani et al., 2015[a]
Random sequence generation	?	?	+	+	?	+
Allocation concealment	?	?	+	?	?	+
Blinding of outcome assessment	?	+	+	+	?	+
Incomplete outcome data	?	+	+	+	?	+
Selective reporting	–	+	+	+	–	–

+ = low risk of bias; ? = unclear risk of bias; – = high risk of bias.
[a] authors provided extra information by e-mail to allow assessment of the risk of bias.

more recent study, in which histograms of gray scale in digital images were measured in WSL/PO, all the treated lesions were masked, with partial (73%) and complete masking results (27%) [25].

In the RCT studies, resin infiltration was compared to non-treatment [27,28,30], remineralization [27,32], or bleaching [33]. The main outcome investigation method was performed by means of digital photographs, analyzed visually or with image processing software, which compared baseline and after treatment color conditions.

Comparing resin infiltration (RI) masking efficacy to the non-treatment control (C) by means of the CIE L*a*b* system, Knösel et al. [28] reported a significant higher color variation for resin infiltration ($\Delta E = 2.55\text{-RI} \times 0.29\text{-C}$). This significant result was also reported by Senestraro et al. [29], with reduction of affected area analysis ($60.9\%\text{-RI} \times 1\%\text{-C}$). When compared to remineralization strategies, distinct results were reported. In the study of Wang et al. [27], a significant reduction of the affected area was obtained for RI (53.5%) compared to fluoride varnish treated lesions (49.2%). In the conference abstract of Haddad et al. [32], both resin infiltration and remineralization with fluoridated dentifrice supplemented with calcium (Novamin) presented a significant decrease in severity of WSL/PO. Compared to bleaching (B), Gugnani et al. [33] reported significantly higher color variation for RI ($\Delta E = 5.53$) than to B only ($\Delta E = 2.53$).

No restrictions were included for follow-up time, which varied from immediate up to 6 months after treatment. The two studies with overlapping results followed the original outcomes up to one year and reported the maintenance of the initial color masking during the evaluation period [26,30].

3.3. Risk of bias within studies

Methodological appraisal of the selected non-randomized studies using MINORS tool is presented in Table 3. The assessment varied from 10 to 14 scores of 16 (maximum global score). All three studies clearly stated the aim of the investigation, reported the prospective collection of data, and properly described the main outcome, as well as the follow-up time. Additionally, no loss of treated subjects in follow-up periods was reported. However, limitations were found for the description of inclusion of consecutive patients, prospective calculation of the study size [24,25], and unbiased assessment of the outcomes (blindness) [24]. Thus, two studies were classified as "moderate quality" [24,25] and one as "high quality" [23].

The assessment of the risk of bias of the RCT studies is presented in Table 4. The items chosen as the key domains in this review were random sequence generation, blinding outcome measurement, and selective reporting. Since studies of Banava and Yazdi, 2011 [31] and Haddad et al., 2014 [32] are conference abstracts and there was no access to additional information from the authors, they were classified as "unclear" or "high" risk of bias in all domains. In the study of Gugnani et al., 2015 [33], the authors provided additional information by e-mail, thus risk of bias was classified as "low" only for the selective reporting domain. Two full-text studies reported the method of randomization employed [28,29], and one did not, which was classified as "unclear" [27]. Regarding the allocation concealment domain, only one full-text study [28] and one abstract [33] reported that sealed opaque envelopes were used. The blinding outcome assessment was reported in all full-text studies [27–29] and in the abstract as Supplementary information given by the authors [33]. Blinding of participants and personnel was not included in the quality assessment, since this was not possible due to the nature of treatments. Incomplete outcome data and selective reporting were classified as "low" risk of bias for all three full-text studies.

4. Discussion

The resin infiltration concept was developed in the 1970's [34], and since then low viscosity resin materials, such as sealants and adhesives, have been used as attempts to restore decalcified enamel [35,36]. At the end of the 2000's, investigations about etching efficacy over the hypermineralized surface enamel and the development of a material with a higher penetration coefficient, called infiltrant, expanded the clinical use of the technique, both for caries arrestment and masking [8,9].

Since the use of infiltrants for masking enamel whitish discolorations has only spread in more recent years, the amount of clinical studies is limited. Thus, in this review, both non-randomized and RCT design studies were included. RCT studies usually present a lower risk of bias and systematic errors, being considered at the highest quality rating [37]. However, the quality of the study must be assessed to confirm the level of evidence. Distinct quality assessment methods were used, according to the following study designs: MINORS tool for non-randomized studies and Cochrane Risk of Bias tool for RCTs. Based on these methods, different risks of bias for both study designs were identified, that is, two non-randomized studies were considered as "moderate quality" and four RCT studies were classified as "unclear" or "high" risk of bias in the chosen key domains.

Since the resin infiltration technique is similar, independent of the lesion type, the nature of lesions was not used as an exclusion criteria. Overall, the post-orthodontic white spot lesions were the most common treated discoloration reported in the selected studies. This type of lesion represents a common undesirable side effect of patients with fixed orthodontic appliances, as cleaning around the brackets is hampered [3,38]. The regression of demineralized areas has been described as a result of the remineralizing action of saliva and use of remineralizing agents such as fluorides and calcium-based products [3,4]. However, reversal of the enamel optic appearance is extremely difficult and frequently whitish color remains, especially in long-existing lesions [39]. Thus, resin infiltration has been used as an alternative minimally invasive strategy to mask these lesions.

In the selected studies, distinct outcomes were obtained, depending on the evaluation method. In the non-randomized clinical efficacy design studies, digital photographs of the affected enamel were compared by software in order to measure the difference in color before and after treatment, or difference in the affected area. There was a high percentage of completely and partially masked WSL/PO lesions for all three selected studies, with significant differences before and after treatment [23–25]. It must be highlighted that different factors may influence masking outcomes, such as extension, depth, and activity of post-orthodontic lesions [23,25,28]. Other evaluation methods reported in RCT studies were spectrophotometry [28], laser fluorescence [32], and visual analysis [29,31].

Since promising clinical masking results were clinically reported with demineralized enamel, resin infiltration was also employed in enamel developmental defects. Although favorable results were shown in clinical cases and case series [2,20,22], these study designs were not included in this review, since they were not comparative. One clinical efficacy non-randomized study included enamel development defect lesions, resulting from MIH or hypomineralization [23], and two RCT abstracts evaluated fluorotic discolored enamel [21,31]. Despite the promising outcomes, when resin infiltration was used, lower masking efficacy was reported in DDE than in WSL/PO lesions [23]. This may be due to differences in the hystophatology (topographical forms) of the lesions [22]. Nevertheless, more comparative studies must be performed considering the nature and severity of lesions to increase the evidence for the predicted outcome.

When compared to non-treatment, the masking effect of resin infiltration on WSL/PO, measured either with color alteration [28] or with reduction of affected area [29], was significantly evident. This was also observed for fluorotic enamel [31]. In the resin infiltration versus remineralization comparative studies, both strategies significantly reduced whitish appearance of enamel [32], but better esthetic results were reported with resin infiltration [27]. When resin infiltration was compared to bleaching in fluorotic enamel, significantly higher esthetic improvement was obtained with resin infiltration [33].

As the hypermineralized surface layer may differ depending on the demineralized lesion activity [8] and the hystopathology of the different types of DDE lesions [1], the hydrochloric acid (HCl) exposure time may also vary [6], but there is no definite protocol for this procedure. Most of the selected studies reported a 15% HCl application for 2 min, according to the manufacturer's recommendation [23–25,31]. Nevertheless, a longer time of up to 8 min [28] or the association with an abrasion [29] was also reported, in order to maximize the potential for resin infiltration. Thus, since differences in the lesions' characteristics are present, standardization of the technique is difficult and may influence the outcomes of different studies.

Sample size and follow-up time were not used as exclusion criteria, which is different than a previous systematic review of WSL/PO lesions management [38]. In the non-randomized selected studies, prospective calculation of the study size was not described, and the number of treated teeth varied from 38 to 74 (18 to 21 participants). In the RCT selected studies, treated teeth ranged from 20 to 231 (20 to 83 participants). Two full-text split-mouth design RCT studies reported a sample size calculation, described in terms of number of participants [28,29]. Additionally, information about the sample size calculation of the conference abstract [33] was also given by e-mail. The same studies also reported the random sequence generation method, but the allocation concealment method was only reported by Knösel et al. [28] and Gugnani et al. [33]. In the Senestraro et al. [29] split-mouth design study, randomization was performed to determine one non-treated tooth per participant to maximize the number of treated teeth in order to compensate for variations. The remaining teeth were allocated for the treatment group.

Although the longevity of a treatment is a very important variable in clinical studies, the masking effect is usually achieved immediately after resin infiltration. This is a consequence of the penetration of a low-viscosity resin within enamel porosities by capillarity, altering the refractive index of the affected structure [6]. Thus, follow-up time was not considered as an exclusion criterion. In the non-randomized selected studies, the masking effect was evaluated immediately [24] and one week after treatment [23,25]. One study continued the clinical assessment of enamel color change resulting from resin infiltration for one year and observed that the masking effect remained stable after 12 months [26]. Information about this study is presented in the data extraction table, but it was not included in the quality assessment due to overlapping results. Since the previous study [25] presented more complete data and a higher sample size, it was chosen for quality assessment.

In the full-text RCT studies, follow-up assessments were distinct, varying from 8 weeks [29] to 6 months [27,28,31]. There were no significant differences between color changes measured immediately after treatment and after 8 weeks [29] or 6 months [28]. One study continued the follow-up period for up to 12 months [30] and reported that the masking effect observed after 6 months in the previous study [28] persisted after 12 months. This study is also only described in the extraction data table and not in the quality assessment due to overlapping results. Additionally, the sample size was reduced compared to the initial study, due to drop-out of participants.

It has to be highlighted that although the camouflage effect is reported to be immediate, as discussed above, concern exists about the durability of esthetic results due to staining and aging of the low-viscosity resin used for infiltration. This is still a controversial issue in laboratorial studies, with different staining potential reported after immersion in different colored solutions [7,40,41]. Therefore, further clinical trials with long-term assessment periods are necessary in order to demonstrate longevity and to strengthen the evidence for clinical recommendation of the technique.

The blinding of outcome assessment was considered a key domain, since it is important to minimize attrition bias. Nevertheless, blinding of participants and personnel was not viable, due to the different nature of comparison treatments (no treatment [28,29], remineralization [27], or bleaching [33]). Additionally, selective reporting is important to detail the information of the study. Since three studies were conference abstracts, this domain was considered as high risk of bias for them, despite of the attempts to contact the authors.

Notwithstanding the low amount of RCT studies and the methodological variability among them, it is obvious that resin infiltration is a promising technique for enamel white discoloration camouflage. Although the method is technique sensitive and depends on the hystopathological characteristics of the discoloration, reports of total or, at least, partial masking are present in all selected studies. Nevertheless, existing evidence for the technique efficacy is still limited and relies on the lack of long-term studies with a satisfactory sample size.

5. Conclusion

This systematic review, based on scientific information available at the present time, concluded that the resin infiltration technique seems to be a feasible option for color masking of enamel whitish discolorations, resulting both from white spot lesions and enamel development defects. Nevertheless, there is no strong evidence supporting the clinical recommendation of the

technique. Further long-term randomized controlled trials, with a larger sample size and longer follow-up time should be approached to increase this evidence.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jdent.2016.10.010.

References

[1] M. Denis, A. Atlan, E. Vennat, G. Tirlet, J.P. Attal, White defects on enamel: diagnosis and anatomopathology: two essential factors for proper treatment (part 1), Int. Orthod. 11 (2) (2013) 139–165.
[2] C.R. Torres, A.B. Borges, Color masking of developmental enamel defects: a case series, Oper. Dent. 40 (1) (2015) 25–33.
[3] M. Akin, F.A. Basciftci, Can white spot lesions be treated effectively? Angle Orthod. 82 (5) (2012) 770–775.
[4] G.J. Huang, B. Roloff-Chiang, B.E. Mills, S. Shalchi, C. Spiekerman, A.M. Korpak, et al., Effectiveness of MI Paste Plus and PreviDent fluoride varnish for treatment of white spot lesions: a randomized controlled trial, Am. J. Orthod. Dentofac. Orthop. 143 (1) (2013) 31–41.
[5] M. Knösel, R. Attin, K. Beckers, T. Attin, A randomized CIE L*a*b* evaluation of external bleaching therapy effects on fluorotic enamel stains, Quintessence Int. 39 (5) (2008) 391–399.
[6] S. Paris, H. Meyer-Lueckel, Masking of labial enamel white spot lesions by resin infiltration-a clinical report, Quintessence Int. 40 (9) (2009) 713–718.
[7] S. Paris, F. Schwendicke, J. Keltsch, C. Dorfer, H. Meyer-Lueckel, Masking of white spot lesions by resin infiltration in vitro, J. Dent. 41 (Suppl. 5) (2013) e28–e34.
[8] H. Meyer-Lueckel, S. Paris, A.M. Kielbassa, Surface layer erosion of natural caries lesions with phosphoric and hydrochloric acid gels in preparation for resin infiltration, Caries Res. 41 (3) (2007) 223–230.
[9] H. Meyer-Lueckel, S. Paris, Improved resin infiltration of natural caries lesions, J. Dent. Res. 87 (12) (2008) 1112–1116.
[10] F. Crombie, D. Manton, J. Palamara, E. Reynolds, Resin infiltration of developmentally hypomineralised enamel, Int. J. Paediatr. Dent. 24 (1) (2014) 51–55.
[11] A.J. de Lacerda, D.M. Avila, A.B. Borges, C.R. Pucci, C. Rocha Gomes Torres, Adhesive systems as an alternative material for color masking of white spot lesions: do they work? J. Adhes. Dent. 18 (1) (2016) 43–50.
[12] C. Rocha Gomes Torres, A.B. Borges, L.M. Torres, I.S. Gomes, R.S. de Oliveira, Effect of caries infiltration technique and fluoride therapy on the colour masking of white spot lesions, J. Dent. 39 (3) (2011) 202–207.
[13] M.A. Munoz, L.A. Arana-Gordillo, G.M. Gomes, O.M. Gomes, N.H. Bombarda, A. Reis, et al., Alternative esthetic management of fluorosis and hypoplasia stains: blending effect obtained with resin infiltration techniques, J. Esthet. Restor. Dent. 25 (1) (2013) 32–39.
[14] A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gotzsche, J.P. Ioannidis, et al., The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration, Br. Med. J. 339 (2009) b2700.
[15] K. Slim, E. Nini, D. Forestier, F. Kwiatkowski, Y. Panis, J. Chipponi, Methodological index for non-randomized studies (minors): development and validation of a new instrument, ANZ J. Surg. 73 (9) (2003) 712–716.
[16] W. Kahn, M. Khan, H. Alradwan, R. Williams, N. Simunovic, O.R. Ayeni, Utility of intra-articular Hip injections for femoroacetabular impingement: a systematic review, Orthop. J. Sports Med. 3 (9) (2015) 2325967115601030.
[17] J.P. Higgins, D.G. Altman, P.C. Gotzsche, P. Juni, D. Moher, A.D. Oxman, et al., The Cochrane Collaboration's tool for assessing risk of bias in randomised trials, Br. Med. J. 343 (2011) d5928.
[18] Y. Wang, Y. Sa, S. Liang, T. Jiang, Minimally invasive treatment for esthetic management of severe dental fluorosis: a case report, Op. Dent. 38 (4) (2013) 358–362.
[19] T.M. Auschill, K.E. Schmidt, N.B. Arweiler, Resin infiltration for aesthetic improvement of mild to moderate fluorosis: a six-month follow-up case report, Oral Health Prev. Dent. 13 (4) (2015) 317–322.
[20] J.P. Attal, A. Atlan, M. Denis, E. Vennat, G. Tirlet, White spots on enamel: treatment protocol by superficial or deep infiltration (part 2), Int. Orthod. 12 (1) (2014) 1–31.
[21] N. Gugnani, I.K. Pandit, V. Goyal, S. Gugnani, J. Sharma, S. Dogra, Esthetic improvement of white spot lesions and non-pitted fluorosis using resin infiltration technique: series of four clinical cases, J. Indian Soc. Pedod. Prev. Dent. 32 (2) (2014) 176–180.
[22] G. Tirlet, H.F. Chabouis, J.P. Attal, Infiltration, a new therapy for masking enamel white spots: a 19-month follow-up case series, Eur. J. Esth. Dent. 8 (2) (2013) 180–190.
[23] S. Kim, E.Y. Kim, T.S. Jeong, J.W. Kim, The evaluation of resin infiltration for masking labial enamel white spot lesions, Int. J. Paediatr. Dent. 21 (4) (2011) 241–248.
[24] S.M. Hammad, M. El Banna, I. El Zayat, M.A. Mohsen, Effect of resin infiltration on white spot lesions after debonding orthodontic brackets, Am. J. Dent. 25 (1) (2012) 3–8.
[25] C. Feng, R. Liu, R. Liu, Q. Zhao, X. Chu, Effect of infiltration resin on the color masking of labial enamel white spot lesions, West China J. Stomatol. 31 (6) (2013) 597–599.
[26] C.H. Feng, X.Y. Chu, Efficacy of one year treatment of icon infiltration resin on post-orthodontic white spots, J. Peking Univ. Health Sci. 45 (1) (2013) 40–43.
[27] L. Wang, J. Jian, H.F. Lu, Efficiency of resin infiltration versus fluride varnish for treatment of post-orthodontic white spot lesions, Chin. J. Tissue Eng. Res. 17 (29) (2013) 5303–5308.
[28] M. Knösel, A. Eckstein, H.J. Helms, Durability of esthetic improvement following Icon resin infiltration of multibracket-induced white spot lesions compared with no therapy over 6 months: a single-center, split-mouth, randomized clinical trial, Am. J. Orthod. Dentofac. Orthop. 144 (1) (2013) 86–96.
[29] S.V. Senestraro, J.J. Crowe, M. Wang, A. Vo, G. Huang, J. Ferracane, et al., Minimally invasive resin infiltration of arrested white-spot lesions: a randomized clinical trial, J. Am. Dent. Assoc. 144 (9) (2013) 997–1005.
[30] A. Eckstein, H.J. Helms, M. Knösel, Camouflage effects following resin infiltration of postorthodontic white-spot lesions in vivo: one-year follow-up, Angle Orthod. 85 (3) (2015) 374–380.
[31] S. Banava, M. Safaie Yazdi, Effect of resin infiltration technique on enamel fluorosis: preliminary results, J. Dent. Res. 90 (B) (2011).
[32] B. Haddad, T.P. Hope, M. Rampp, A.R. Jordan, Treatment of white spot lesions after fixed orthodontic appliance (RCT), J. Dent. Res. 93 (C) (2014).
[33] N. Gugnani, I. Pandit, S. Gugnani, M. Gupta, S. Soni, V. Juneja, et al., Evaluation of esthetic improvement of non-pitted fluorosis using CIELAB parameters and patient satisfaction, when treated with resin infiltration, bleaching and bleaching with resin infiltration, J. Dent. Res. 94 (A) (2015).
[34] C. Robinson, A.S. Hallsworth, J.A. Weatherell, W. Kunzel, Arrest and control of carious lesions: a study based on preliminary experiments with resorcinol-formaldehyde resin, J. Dent. Res. 55 (5) (1976) 812–818.
[35] T.P. Croll, Bonded resin sealant for smooth surface enamel defects: new concepts in microrestorative dentistry, Quintessence Int. 18 (1) (1987) 5–10.
[36] S. Paris, H. Meyer-Lueckel, A.M. Kielbassa, Resin infiltration of natural caries lesions, J. Dent. Res. 86 (7) (2007) 662–666.
[37] P.B. Burns, R.J. Rohrich, K.C. Chung, The levels of evidence and their role in evidence-based medicine, Plast. Reconstr. Surg. 128 (1) (2011) 305–310.
[38] M. Sonesson, F. Bergstrand, S. Gizani, S. Twetman, Management of post-orthodontic white spot lesions: an updated systematic review, Eur. J. Orthod. (2016), doi:http://dx.doi.org/10.1093/ejo/cjw023 (in press).
[39] C. Zantner, P. Martus, A.M. Kielbassa, Clinical monitoring of the effect of fluorides on long-existing white spot lesions, Acta Odontol. Scand. 64 (2) (2006) 115–122.
[40] F. Cohen-Carneiro, A.M. Pascareli, M.R. Christino, H.F. Vale, D.G. Pontes, Color stability of carious incipient lesions located in enamel and treated with resin infiltration or remineralization, Int. J. Paediatr. Dent. 24 (4) (2014) 277–285.
[41] A. Borges, T. Caneppele, M. Luz, C. Pucci, C. Torres, Color stability of resin used for caries infiltration after exposure to different staining solutions, Oper. Dent. 39 (4) (2014) 433–440.