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Restorative Treatment in Patients with Amelogenesis Imperfecta: A Review

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Keywords
Adhesive; ceramic; enamel dysplasia; hereditary disorder; rehabilitation; resin-based composite; restoration.

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Abstract

Purpose: To summarize the contemporary scientific evidence available regarding restorative dental treatment in patients with Amelogenesis imperfecta (AI).
Methods: An electronic literature search was conducted using the search term "Amelogenesis imperfecta" and the PubMed/MEDLINE database as well as Google Scholar. Prospective and retrospective clinical studies that investigated the outcome of direct and/or indirect dental restorative treatment in patients with AI, were published in English, and had an observation time of at least 1 year were included in this review. The articles identified were screened and analyzed by two reviewers according to inclusion and exclusion criteria in three review rounds.
Results: Six prospective or retrospective clinical studies analyzing longevity and complications associated with dental restorative treatment in patients with AI met the inclusion criteria. Extracted data suggest that in patients with AI, indirect restorations feature superior predictability and longevity than direct restorations.
Conclusions: As endodontic complications were infrequently observed and periodontal parameters regularly improve with the insertion of indirect restorations, dental treatment in patients with AI should focus on indirect restorations as soon as possible. While adhesive bonding techniques to enamel surfaces in patients with AI feature merely limited predictability and longevity and as the available data is scarce, further laboratory and clinical studies should be performed to investigate the performance of minimally invasive indirect restorations bonded to enamel in patients with AI. *Recommendation:* Scientific evidence indicates that indirect restorations should be preferred over direct restorations in patients with AI.

Amelogenesis imperfecta (AI) is an infrequent hereditary developmental disorder primarily affecting the enamel tooth tissues. Mutation or changed expression of 13 genes have been identified as causative agents for AI, including AMELX, ENAM, MMP20, KLK4, FAM83H, WDR72, FAM20A, SLC24A4, DLX3, AMBN, LAMB3, ITGB6, and C4orf26; in addition, the role of ALB and TUFT1 is still discussed.[1,2] The mode of AI inheritance is either autosomal dominant, autosomal recessive, or X-linked.[3] International studies investigating the prevalence of AI estimate that its prevalence is lower than 0.5%.[4] However, data indicate that the prevalence of AI varies between countries, as prevalences of 43/10000 in Turkey,[5] 4/1000 in Sweden,[6] and 1/14000 in the United States have been reported.[7]

In the past, numerous classifications of AI deriving from the enamel phenotype, the mode of inheritance, molecular defects, and biochemistry have been introduced.[8] As AI is based on clinical and radiographic criteria, classification according to the enamel phenotype appears to be the most suitable for the dental clinician. It includes a hypoplastic (class I), hypomaturated (class II), hypocalcified (class III), and a hybrid type with signs of both hypomatured and hypoplastic enamel as well as taurodontism (class IV),[9] which might be sub-classified into different subtypes for each phenotype.[9] In instances of hypoplastic AI, the thickness of the enamel layer is reduced, and enamel tissues can be radiographically distinguished from dentine.[9] In hypomaturated AI, the enamel layer features a physiological thickness, but appears mottled and softer than sound enamel; radiopacity is similar to dentine.[9] The thickness of the enamel layers is physiological in cases of hypocalcified AI, yet due to the impaired calcification the enamel surfaces are subject to increased wear.[9] Radiographically, enamel appears less radiopaque than dentine.[4,9]

While the psychosocial impact of AI is significant,[10] adolescent patients demand functional and esthetic rehabilitation.[11]

Treating patients with AI, dentists may be confronted with various dental abnormalities, including follicular cysts, delayed eruption, and retention and impaction of teeth as a result of the impact of AI on the eruptive process of the permanent teeth.[12] Taurodontism and reduced crown size are regularly observed in patients with AI; other frequent findings include enlarged pulp chambers, intrapulpal calcifications, pulp stones, crown resorptions, and agenesis.[12] Moreover, patients with AI regularly suffer from gingival and periodontal inflammation, which may coincide with poor oral hygiene and calculus.[12] With regard to occlusion, malocclusion is a frequently observed condition in patients with AI; numerous patients suffer from open bite.[12] Other functional problems in patients with AI include tooth hypersensitivity, increased wear, short clinical crowns, and loss of occlusal vertical dimension. Esthetic concerns relate to the impaired color and appearance of the anterior teeth.[13]

Both direct and indirect treatment options are regularly suggested for the restorative rehabilitation of patients with AI; however, the conventional wisdom is to postpone the rehabilitation of adolescents with AI with indirect restorations for preventing potential endodontic complications. Indirect treatment options include minimally invasive methods such as veneers and partial coverage restorations or classical treatment approaches such as crowns and fixed dental prostheses (FDPs). Depending on the indication, composite and ceramic materials as well as alloys may be used for the fabrication of the indirect restorations. Implant therapy is another option in patients with AI and missing teeth.[13] Depending on the enamel phenotype, clinical problems in the dental treatment of patients with AI include problematic adhesive bonding to enamel surfaces, as qualitative changes in the composition of enamel in patients with AI account for impaired bond strength between enamel and resin. With regard to this aspect, Yaman et al observed an almost 40% lower microtensile bond strength of etch-and-rinse and self-etch adhesives to enamel affected by hypoplastic AI in comparison to sound enamel.[14] For enamel affected by hypocalcified AI, Faria-e-Silva et al discovered a similar decrease in the microshear bond strength of an etch-and-rinse adhesive.[15]

Although countless clinical reports and several scientific studies addressing dental treatment in with AI have been published, no commonly accepted guidelines for the treatment of patients with AI have been introduced. Confining their literature search to randomized controlled clinical trials, Dashash et al failed to identify high-level clinical studies investigating the outcome of direct and indirect dental restorative treatment in patients with AI and to derive guidelines.[16] However, the difficulties for the clinician to identify the most appropriate treatment options for the rehabilitation of patients with AI remain. Thus, the aim of the present review was to screen and summarize the scientific literature available and to derive evidence-based restorative treatment options for the rehabilitation of patients with AI from prospective and retrospective clinical studies.

Methods

Search methodology

A systematic literature search was conducted between February and May 2016 including articles in English published or in press in journals indexed in the free digital archive of PubMed, using the query term "Amelogenesis imperfecta." The reference lists of the initially retrieved studies were hand searched for potentially relevant articles. Related links were also considered. A comprehensive online literature search using Google Scholar was additionally performed using the query term "Amelogenesis imperfecta."

Study selection

Titles and abstracts of the articles identified by the electronic search were read and assessed by two authors (SS, SH). In cases of ambiguous titles and abstracts or in cases where no abstract was available, the full text of the article was retrieved and screened. First-round exclusion criteria included articles that did not relate to dental treatment in patients with AI. Articles that met first-round inclusion criteria were retrieved in full and reviewed according to the second-round inclusion criteria, excluding studies addressing genetic, histological, and psychological aspects in patients with AI, alternative medicine, syndromes, and other miscellaneous aspects rather than dental restorative treatment. Third-round review excluded all clinical reports. In addition, clinical studies that did not report case numbers or details on the restorative treatment performed or reported observation times lower than 1 year were also excluded.

Data extraction

Details from the articles included in this systematic review were extracted independently by two authors (SS, SH). Any potential conflict was resolved by discussion between the authors.

Results

The electronic search using PubMed identified a total of 894 articles, the titles and abstracts of which were screened for first-round inclusion. From these, 738 articles were judged irrelevant and were discarded. The reference lists of the remaining 156 articles were hand-searched for additional relevant articles and supplemented by the comprehensive online literature search, identifying 121 relevant articles. A total of 277 articles were forwarded to second-round screening, where review articles (44), articles relating to genetic (40), histological (27), and psychological (4) aspects in patients with Amelogenesis imperfecta, alternative medicine (4), syndromes (44), and miscellaneous (12) aspects were excluded. One hundred and two (102) relevant manuscripts were assessed in the third-round review, where clinical reports (92) and two clinical studies were excluded. A final total of six relevant clinical studies investigating dental restorative treatment in patients with AI were included in the review. Characteristic details were extracted and are summarized in Table 1.

The data gathered in the literature indicate that the vast majority of clinical data regarding dental restorative treatment in patients with AI have been published in clinical reports. Although numerous clinical reports doubtlessly document successful and impressive dental treatments in patients with AI, well-designed clinical studies are necessary to establish evidence-based and commonly accepted guidelines for the treatment of patients with AI. As blinding is almost impossible

Table 1 Details on clinical studies included in this review

Study	*N* (patients)	Age of patients treated (range)	Type of Amelogenesis imperfecta treated	*N* (teeth or patients per type of AI)	Type of restoration	Observation time (mean; years)	Characteristics
Pousette Lundgren et al, 2015[26]	27	11-22	Hypoplastic Hypomineralized/ hypmaturated Hypomaturated Hypocalcified AI with taurodontism	151 teeth 76 teeth 10 patients 1 patient 1 patient	Indirect (crowns)	2-5	- randomized, controlled study - comparison of the longevity of two types of all-ceramic crowns in patients with AI - split-mouth approach - 108 IPS e.max Press crowns, 119 Procera crowns
Pousette Lundgren et al, 2014[17]	82	6-25	Hypoplastic Hypocalcified/ hypomaturated	38 patients 44 patients	Direct indirect (crowns, veneers, partial coverage restorations)	6-12	- cross-sectional, retrospective study - comparison of oral health and longevity of restorations in patients with AI and control group - no detailed information on the observation time was given - indirect restorations were prepared from Procera (120 crowns), IPS e.max Press (132 crowns), and Empress (45 veneers, partial coverage restorations, crowns)
Chen et al, 2013[18]	8	9-15	Hypoplastic Hypocalcified Hypoplastic/ hypomaturated	4 patients 2 patients 2 patients	Direct indirect (veneers, crowns)	3.2	- restoration of 74 teeth (31 molars, 36 incisors) in patients with AI using various direct and indirect methods and restorative materials, including steel crowns, amalgam, resin-based composite, resin crowns/veneers
Sönmez et al, 2009[24]	4	8-11	Hypocalcified	32 teeth	Direct	3	- prospective trial with split-mouth approach to compare the effect of deproteinization in patients with hypocalcified AI on the longevity of directly manufactured composite crowns
Krieger et al, 2009[27]	5		n/a	99 teeth	Indirect (crowns, FDPs)	18.3 (median)	- retrospective analysis of the prevalence of technical and biological complications in indirect restorations in young patients with birth defects - patients with lip and palate clefts, amelogenesis/dentinogenesis imperfecta, and hypodontia/oligodontia were included - data in left columns were extracted from the publication for patients with amelogenesis/dentinogenesis imperfecta - no specific information on complications regarding indirect restorations in patients with AI are reported - no details on the restorative materials used available
Lindunger and Smedberg, 2005[11]	15	14-37	Hypoplastic Hypocalcified	10 patients 5 patients	Indirect (crowns, onlays/inlays, veneers)	5	- retrospective study - analysis of the outcome of prosthetic treatment in patients with AI - analysis of attitude of patients to prosthetic treatment - 10 alloy crowns, 121 metal-ceramic crowns, 28 ceramic crowns, 18 porcelain onlays/veneers, 36 porcelain veneers

in prospective clinical studies investigating different treatment approaches in dentistry, and as only six relevant clinical studies could be identified and included in the current review, further clinical and (due to the low prevalence of AI) prospective multicenter studies for clarifying the performance of direct and indirect dental restorations in patients with AI are necessary.

Discussion

Direct restorations

While AI regularly affects both primary and secondary teeth, the clinical studies published on restorative treatments were primarily conducted in secondary teeth. Direct restorations with resin-based composites are commonly preferred in young patients for avoiding extensive preparation of teeth during adolescence; however, the data strongly suggest that with a 5-year-survival rate of 50%, the longevity of direct restorations made from resin-based composite and glass ionomer cements is significantly lower in patients with AI than in matching healthy control groups, where a 5-year-survival rate of 80% was observed. As a result, in $9.5 \pm 15.7\%$ of patients with AI visits to the dental clinic, restorations had to be replaced, compared to $1.9 \pm 5.0\%$ in the control group.[17] While the reasons for failure of direct restorations in the control group included secondary caries (35%), loss or fracture of restoration and/or teeth (27%) as well as trauma and endodontic complications (17%), loss or fracture of restauration and/or tooth was more frequently identified as a reason for the replacement of direct restorations in the AI group (63%), followed by secondary caries (14%), tooth sensitivity problems (12%), or trauma (2%).[17] Similar results have been published by other groups, who investigated the performance of stainless steel crowns and amalgam restorations in posterior and direct and indirect resin-based composite restorations in anterior teeth over a mean observation time of 38.5 months, identifying a failure rate of direct restorations of 52% and of stainless steel crowns of 4%.[18] Unfortunately, the authors of this study provided no details regarding materials and treatment procedures employed. Nevertheless, these clinical observations underline the clinical problems associated with adhesive bonding to enamel in patients with AI and support the results of laboratory studies on adhesive bond strength to AI-affected enamel, which reported impaired bond strength of etch-and-rinse and self-etch adhesives to enamel affected by hypoplastic or hypocalcified AI and observed relevant morphological differences between sound and AI-affected enamel surfaces after etching with orthophosphoric acid and self-etching primers.[14,15,19]

Interestingly, a group from Sweden reported a significantly lower survival rate of direct restorations in patients with severe cases of AI or those with hypomineralized/hypomaturated forms of AI than in patients with moderate cases of AI or hypoplastic forms of AI,[17] suggesting that correct classification of AI is an essential part in the diagnostic algorithm and relevant for the clinical treatment. In contrast to these clinical observations, data gathered in laboratory research regarding the adhesive bond strength to AI-affected enamel allow no simple relation between bond strength and the various classes of AI, as the differences observed result from variations in the experimental design employed and the severity of AI rather than differences in the histological features of the affected enamel.[14,15] However, regarding adhesive bonding to enamel in patients with AI, some recent clinical reports highlighted that direct and adhesively bonded restorations can feature favorable long-term results,[20,21] which might be a result of the continuous improvement of bonding systems in recent years.

For improving adhesive bonding to enamel in patients with hypocalcified AI, Sönmez et al[24] employed a deproteinization procedure with 5% sodium hypochlorite prior to adhesive cementation of directly manufactured resin-based composite strip crowns. Previous studies had highlighted that enamel in patients with hypocalcified AI features a higher protein content than regular enamel,[22,23] which might negatively affect adhesive bond strength. Although Sönmez et al failed to identify significant differences in the longevity of the restorations after an observation time of 36 months, they reported less pronounced marginal discoloration in restorations on teeth that had been treated with sodium hypochlorite prior to restoration, suggesting an improved bonding procedure.[24] However, results from laboratory studies investigating the effect of a sodium hypochlorite deproteinization procedure on the adhesive bond strength to enamel affected by hypocalcified AI reported ambiguous results.[15,25]

Indirect restorations

In contrast to direct restorations, the type of AI appears to be irrelevant for the longevity of indirect restorations. Data gathered in a high-quality prospective study by Pousette Lundgren et al[26] as well as retrospective data published by Lindunger and Smedberg[11] indicated no significant difference in the longevity of indirect restorations in patients with various types of AI. Overall, the available clinical studies agree that indirect restorations in patients with AI feature predictable success rates and excellent longevity.

Older publications mostly investigated the performance of alloy or veneered alloy restorations. After a median of 5 years of clinical service, Lindunger and Smedberg rated 212 of 213 restorations as satisfactory or excellent.[11] Krieger et al identified that 4 of 5 patients with AI experienced failures within a median observation time of 18.3 years, which was attributed to the exchange of 26 of 92 crowns for esthetic rather than functional reasons.[27]

More recently published studies supplied patients with all-ceramic rather than metal-based restorations; in their prospective split-mouth trial Pousette Lundgren et al identified that after 2 years of observation more than 97% of the all-ceramic crowns inserted showed at least satisfactory clinical quality, observing no significant differences between two types of all-ceramic restorative materials (Procera [veneered zirconia] and IPS e.max press [lithium disilicate ceramic]).[26] Similar results had been published in a previous study from the same group, gathering data from dental records and a single clinical examination.[17]

While for crown restorations the excellent longevity observed is most likely due to the extensive removal of the irregular AI-affected enamel layer in circumferential preparations, conflicting data have been reported regarding the performance of adhesively bonded all-ceramic restorations such as inlays, onlays, and veneers. While Lindunger and Smedberg[11] reported

no increased failure rates in adhesively bonded all-ceramic inlays, onlays, and veneer all-ceramic restorations, Pousette Lundgren and Dahllöf[17] observed that merely 75% of veneer, partial coverage, or crown restorations made from Empress showed acceptable clinical quality. Unfortunately, detailed information on the preparation designs as well as cementation procedures or the mode of failures were not published in either of the two studies; thus, it cannot be adequately inferred whether the reduced longevity was associated with patient-associated parameters such as AI or material-/protocol-associated factors.

Regarding cementation, data from existing studies highlighted that, regardless of conventional or adhesive cementation protocols, loss of retention of indirect restorations in patients with AI is an infrequent event.[11,17,26] As in the published studies, full-crown preparations have most commonly been employed for the rehabilitation of patients with AI. This phenomenon might be due to the almost complete removal of irregular enamel and additional mechanical retention. Laboratory studies addressing the adhesive bond strength to AI-affected enamel and dentin identified significantly higher adhesive bond strength to dentin in comparison to enamel from AI-affected patients, although values were still significantly lower than for dentin from healthy teeth.[15] These observations suggest that in cases where the irregular enamel layers are removed, indirect restorations might be effectively luted with adhesive cements in AI-affected teeth; however, using SEM analyses, Sanchez-Quevedo et al showed that the dentin in patients with hypocalcified AI was also affected by the disease and was characterized by thickening of the peritubular dentin and partial obliteration of the dentin tubules.[28] While this morphological appearance resembles sclerotic dentin, it has been reported that adhesive bond strengths to sclerotic dentin are lower than to normal dentin as a result of tubular occlusion by mineral salts.[29] These observations might explain the lower adhesive bond strength to dentin of AI-affected teeth; however, as modern prosthetic approaches follow minimally invasive maxims, complete removal of enamel is not necessarily mandatory in patients with AI. Against the background of the high frequency reported for failures of direct restorations as well as the conflicting data for minimally invasive restorations in patients with AI, the effect of different modes of adhesive cementation of indirect restorations should be more thoroughly addressed in further laboratory and clinical studies.

As patients with AI are frequently and in many cases very early supplied with indirect restorations, it is frequently argued that this procedure might cause endodontic complications as a result of the large juvenile pulp tissues; however, data from the clinical studies included in this review indicate that the number of endodontic complications in patients with AI who had been supplied with indirect restorations is low, strongly suggesting that the risk for endodontic complications is overestimated. Pousette Lundgren et al reported that 2 years after supplying patients with AI with a crown, tooth sensitivity decreased in 24 of 27 patients, whereas increased sensitivity was observed in three patients suffering from either pulpitits or apical periodontitits, or without detectable clinical endodontic complication.[26] While an overall prevalence of endodontic complications of 3% was identified, dental trauma prior to or after restorative treatment appeared to be a relevant predictor for endodontic complications.[17] While the observation time was rather low in this study, Lindunger and Smedberg reported a prevalence of endodontic complications of 1% after 60 months of observation.[11]

Regarding periodontal parameters, data reported by Pousette Lundgren et al suggested that gingival inflammation as determined by gingival bleeding indices reduced significantly after restorative therapy with all-ceramic crowns.[26] While this group failed to identify differences in the periodontal parameters between various types of AI, Lindunger and Smedberg reported that periodontal parameters were worse in patients with hypomineralized AI than those with hypoplastic AI.[11] Chen et al reported that plaque indices were worse in sites supplied with direct restorations than in those supplied with indirect restorations.[18]

Secondary caries was infrequently observed in indirect restorations in patients with AI. Lindunger and Smedberg reported that 5% of the restorations inserted showed secondary caries and had to be replaced; however, as the phenomenon severely affected a single patient with 11 crowns needing to be replaced,[11] it appears that the high frequency can be attributed to individual reasons rather than AI. The Pousette Lundgren group reported no instances of secondary caries in both studies.[17,26]

Apart from the analyses of direct and indirect restorations in patients with AI, some researchers also addressed patient satisfaction with the inserted restorations. Data indicated that patients showed a high level of self-reported satisfaction with direct and indirect restorations. In particular, improvement in esthetics and the decrease in tooth sensitivity were appreciated.[11,18] Lindunger and Smedberg reported that 50% of the patients interviewed remarked that they wished that treatment with indirect restorations had started before the age of 16.[11]

Conclusions

Although the number of well-designed clinical studies is limited, the authors attempt to derive some guidelines for the restorative treatment of patients with AI from the clinical studies that could be included into this review:

1. Generally, the data indicate that indirect restorations feature superior predictability and longevity than direct restorations, which is particularly due to the impaired adhesive bonding to AI-affected enamel.
2. While endodontic complications are infrequently observed, rehabilitation of patients with AI employing indirect restorations should commence as early as possible.
3. For rehabilitation with crowns and FDPs, the type of AI appears to be irrelevant. In addition, all-ceramic restorations feature longevity similar to alloy or veneered alloy restorations; however, while minimally invasive treatment concepts are increasingly employed in modern prosthetic dentistry, the performance of adhesive cementation of minimally invasive all-ceramic restorations in patients with AI should be addressed in further laboratory and clinical studies.

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