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EVIDÊNCIAS SOBRE O DIAMINO FLUORETO DE PRATA: ENSINO NO BRASIL E INFLUÊNCIA EM PARÂMETROS RESTAURADORES

Santa Maria, RS
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Tese apresentada ao Curso de Doutorado do Programa de Pós-Graduação em Ciências Odontológicas, Área de concentração em Odontologia, ênfase em Odontopediatria, da Universidade Federal de Santa Maria (UFSM, RS), como requisito parcial para obtenção do grau de **Doutor em Ciências Odontológicas**.

Orientadora: Prof. Dra. Rachel de Oliveira Rocha

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DEDICATÓRIA

Dedico este trabalho às pessoas mais importantes da minha vida!

Com amor, aos meus pais, Jorge e Valúzia.

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A Deus, pela dádiva da vida e por iluminar meu caminho.

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"A companhia." disse o Pequeno Dragão

"O que vale na vida não é o ponto de partida e sim a caminhada.

Caminhando e semeando, no fim terás o que colher."

Cora Coralina

RESUMO

EVIDÊNCIAS SOBRE O DIAMINO FLUORETO DE PRATA: ENSINO NO BRASIL E INFLUÊNCIA EM PARÂMETROS RESTAURADORES

AUTORA: Tatiana Tambara Fröhlich
ORIENTADORA: Rachel de Oliveira Rocha

A presente tese é composta por três artigos científicos, cujos temas principais são o ensino do diamino fluoreto de prata (DFP) e as consequências do seu uso nos tecidos dentários e restaurações subsequentes ao seu uso. Artigo 1: *Teaching and use of silver diamine fluoride in pediatric dentistry: questionnaire-based cross-sectional analysis of undergraduate Brazilian dental schools*. O objetivo deste trabalho foi apresentar um panorama atual do ensino e utilização do DFP nas disciplinas de Odontopediatria dos Cursos de Graduação em Odontologia brasileiros. Questionários foram enviados por correio eletrônico aos professores responsáveis pela disciplina com questões relativas ao ensino e uso de DFP. Os dados obtidos foram analisados descritivamente e por meio do teste do qui-quadrado. Na maioria dos cursos avaliados o DFP é tópico de aulas teóricas, porém seu uso na prática clínica é pouco frequente. O DFP tem sido utilizado principalmente em lesões de cárie cavitadas em dentes decíduos de crianças de 0 a 3 anos, com uso restrito aos dentes posteriores em uma grande parcela dos cursos de graduação. Artigo 2: *Bonding of glass-ionomer cement and adhesive systems to silver diamine fluoride-treated dentine: an updated systematic review and meta-analysis.* Este estudo atualizou uma revisão sistemática sobre a influência da aplicação prévia de DFP na adesão de materiais de sistemas adesivos (SA) e cimento de ionômero de vidro (CIV) à dentina hígida ou afetada por cárie. Onze novos estudos foram somados aos 11 estudos previamente incluídos e 21 estudos foram considerados na meta-análise. O pré-tratamento dentinário com DFP não influenciou na adesão do CIV independentemente da condição da dentina. O tratamento com DFP prejudica significativamente a resistência de união dos SA. No entanto, a etapa de enxágue após aplicação do DFP elimina esse efeito negativo na dentina hígida e pode aumentar a adesão à dentina afetada por cárie. Artigo 3*: Evaluation of the use of potassium iodide application on stained demineralized dentin under resin composite following silver diamine fluoride application.* Este estudo avaliou o efeito do iodeto de potássio (KI) após a aplicação de DFP na coloração da dentina desmineralizada recoberta ou não por uma camada de resina composta. Para isso, 30 blocos de dentina foram preparados, desmineralizados e alocados aleatoriamente em três grupos (n=10): 1) controle (sem tratamento); 2) tratado com DFP; e 3) tratado com DFP e KI. Metade dos espécimes de cada grupo foi recoberto por uma camada de resina composta imediatamente após o tratamento. Os parâmetros de cor foram avaliados, com auxílio de um espectrofotômetro, no início do estudo e após 7, 14, 30 e 60 dias. Os dados foram analisados por meio de modelo linear generalizado. O uso de KI subsequente ao DFP minimiza o escurecimento da dentina e evita o manchamento da dentina sob restaurações de resina composta em longo prazo. O DFP é tópico de ensino nos cursos de graduação em Odontologia do país e seu uso não interfere na adesão de SA e CIV e, associado ao KI, na cor de restaurações de resina composta.

Palavras-chave: Adesivos Dentinários. Cariostáticos. Cor. Ensino. Odontopediatria

ABSTRACT

EVIDENCE ON SILVER DIAMINE FLUORIDE: TEACHING IN BRAZIL AND INFLUENCE ON RESTORATIVE PARAMETERS

AUTHOR: Tatiana Tambara Fröhlich
ADVISOR: Rachel de Oliveira Rocha

This thesis comprises three studies focusing on silver diamine fluoride (SDF) teaching and use, and its effect on dental tissues and restorations after its use. Article 1: Teaching and using silver diamine fluoride in pediatric dentistry: a questionnaire-based cross-sectional analysis of undergraduate Brazilian dental schools. The aim of this study was to present an overview of the teaching and use of SDF in the in Pediatric Dentistry in undergraduate Brazilian dental schools. Questionnaires with questions regarding the teaching and use of SDF were sent by e-mail to the responsible for Pediatric Dentistry courses. The data obtained were analyzed descriptively and using the chi-square test. In most of the evaluated courses, SDF theoretical class topic, but its use in clinical practice is infrequent. SDF has been used mainly in cavitated caries lesions in primary teeth of children aged 0 to 3 years, with its use is restricted to posterior teeth. Article 2: Bonding of glass-ionomer cement and adhesive systems to silver diamine fluoride-treated dentine: an updated systematic review and meta-analysis. This study updated a systematic review on the influence of the previous application of SDF on the bonding or adhesive systems (AS) and glass ionomer cement (GIC), to sound and caries-affected dentin. Eleven new studies were added to the 11 previous studies, and 21 studies in the meta-analysis. Dentin pretreatment with SDF did not influence GIC adhesion, regardless of dentin condition. Treatment with SDF significantly impaired the bond strength of SA. However, the rinsing step after SDF application eliminates this negative effect on sound dentin and may increase the adhesion to caries-affected dentin. Article 3: Evaluation of the use of potassium iodide application on stained demineralized dentin under resin composite following silver diamine fluoride application. This study evaluated the effect of potassium iodide (KI) after the SDF on the staining of demineralized dentin covered or not by a layer of composite resin. For this, 30 dentin blocks were prepared, demineralized, and randomly allocated into three groups (n = 10): 1) control (without treatment); 2) treated with SDF, and 3) treated with SDF and KI. Half of the specimens in each group received a composite resin restoration immediately after treatment. The color parameters were evaluated, with a spectrophotometer, at the beginning of the study and after 7, 14, 30, and 60 days. The data were analyzed using a generalized linear model. The use of potassium iodide minimizes the darkening of dentin and prevents the staining of the dentin under composite resin restorations in the long-term. SDF is a teaching topic in undergraduate Pediatric Dentistry schools in Brazil, and its use does not interfere in the adhesion of SA and CIV and, associated with KI, in the color of composite resin restorations.

Keywords: Cariostatic Agents. Color. Dentin-Bonding Agents. Pediatric dentistry. Teaching

SUMÁRIO

INTRODUÇÃO

O diamino fluoreto de prata (DFP) tem sido considerado um dos tratamentos mais eficazes para paralisação de lesões de cárie, principalmente em dentes decíduos (CHIBINSKI et al., 2017). Seu uso foi proposto no Japão na década de 70 (NISHINO et al., 1969; YAMAGA, YOKOMIZO 1969) e posteriormente passou a ser utilizado em outros países, incluindo o Brasil (CHU CH, LO EC 2008). Recentemente, voltou a ganhar destaque principalmente após sua introdução no mercado americano (HORST et al., 2016), tornando-se, desde então, foco de inúmeras investigações científicas.

O mecanismo de ação do DFP está baseado nos dois principais constituintes, o fluoreto de sódio e o nitrato de prata (MEI et al., 2017). Quando reage com a hidroxiapatita em meio alcalino ocorre a formação de fluoreto de cálcio e fosfato de prata (YAMAGA et al., 1972; AMERICAN ACADEMY OF PEDIATRIC DENTISTRY 2017), sendo o primeiro responsável por promover a remineralização da estrutura dentária e o segundo, por proporcionar ação antibacteriana e efeito inibitório da degradação da matriz orgânica, através da ação dos íons prata (CHU et al., 2012; MEI et al., 2013; ZHAO et al., 2017a).

Apesar dos benefícios atribuídos ao DFP, uma desvantagem inerente ao seu uso é tornar enegrecidas as áreas tratadas (LLODRA et al., 2005). A observação clínica de que o DFP causa o escurecimento da estrutura dentária comprometida pode ser um impedimento significativo para seu uso, trazendo uma grande preocupação estética, especialmente quando os dentes anteriores estão envolvidos (CRYSTAL et al., 2017). O efeito antiestético associado a paralisação da lesão de cárie ainda é considerado preocupante, pela dúvida acerca da aceitação dos pais ou responsáveis, limitando sua aplicabilidade (NELSON et al., 2016). Isso pode fazer com que, apesar dos resultados favoráveis obtidos nas recentes investigações científicas, sua utilização não seja considerada uma opção de tratamento, podendo inclusive, não ser incluído como tópico de ensino nos cursos de graduação país. No Brasil, informações sobre ensino e uso do DFP nos cursos de Odontologia, ainda são inexistentes ou não estão disponíveis.

Recentemente, além do tradicional uso para tratamento de lesões de cárie, a aplicação do diamino fluoreto de prata antes de uma restauração tem sido sugerida. Acredita-se que essa aplicação prévia possa prevenir a formação de lesão de cárie recorrente (WU et al., 2016; WANG et al., 2016; KUCUKYLMAZ et al., 2016) devido as suas propriedades antibacterianas e de remineralização. Estudos laboratoriais demostram que restaurações realizadas após aplicação prévia de DFP são mais resistentes a formação de lesões de cárie quando foram submetidas ao desafio cariogênico (MEI et al., 2016; ZHAO et al., 2017b; OSAMA et al.,

2018), sugerindo assim, que o DFP possa ser incorporado ao protocolo restaurador para melhorar a taxa de sucesso das restaurações.

É sabido, contudo, que qualquer agente aplicado à dentina antes de um procedimento restaurador pode interferir na adesão. Uma camada de fosfato de prata é formada na superfície dentinária tratada com DFP (PATEL et al., 2018) e partículas de prata se estendem para os túbulos dentinários, causando sua obstrução total ou parcial (MEI et al 2013, SAYED et al.,2018), o que pode prejudicar a adesão dos materiais restauradores. Em revisão sistemática com meta-análise (FRÖHLICH et al., 2020) foi observado que a aplicação de DFP não influencia negativamente na resistência de união do cimento de ionômero de vidro à dentina. Diferentemente, pode prejudicar a resistência de união dos sistemas adesivos, sendo, contudo, a etapa de enxágue com água imediatamente após a aplicação do DFP capaz de eliminar esse efeito adverso. No entanto, poucos foram os estudos que consideraram a aplicação de DFP em dentina afetada por cárie, impossibilitando, portanto, a realização da meta-análise com esse subgrupo. Piores resultados podem ser esperados na dentina afetada por cárie, uma vez que diferenças químicas e morfológicas, como menor conteúdo mineral (ANGKER et al., 2004) e aumento da porosidade da dentina intertubular (NAKAJIMA et al., 2005), prejudicam a adesão à este substrato (ISOLAN et al., 2018). Além disso, é essencial considerar que níveis mais elevados de precipitado de prata são formados na dentina desmineralizada em comparação com a dentina hígida (KNIGHT et al., 2007). Após a publicação dessa revisão sistemática outros estudos foram publicados, incluindo agora avaliações em dentina afetada por cárie (VAN DUKER et al., 2019; BRAZ et al., 2020; FIROUZMANDI et al., 2020; JIANG et al., 2020; NG et al., 2020; SIQUEIRA et al., 2020; UCHIL et al., 2020), sem, no entanto, existir consenso entre eles. Portanto, a atualização dessa sistemática revisão prévia, considerando dados dos estudos recentes, se faz necessária.

Ainda sobre a aplicação de diamino fluoreto de prata previamente a uma restauração, uma desvantagem esperada é o provável manchamento das mesmas. Novas, investigações acerca do DFP tem sido realizadas na busca de alternativas para eliminar ou minimizar o seu potencial de manchamento da dentina afetada por cárie e possivelmente também das restaurações realizadas imediatamente após a sua aplicação. A utilização de uma solução de iodeto de potássio (KI) subsequente à sua aplicação tem sido sugerida (KNIGHT et al., 2005; MEI et al., 2018). Estudos anteriores confirmam que o potencial de coloração do DFP é modificado quando a solução KI é utilizada (NGUYEN et al., 2017; PATEL et al., 2018; SAYED et al., 2018; ESPÍNDOLA-CASTRO et al., 2020). No entanto, em alguns desses estudos (SAYED et al., 2018; ESPÍNDOLA-CASTRO et al., 2020) os produtos foram

aplicados em dentina hígida, e sabe-se que uma maior concentração de precipitado é formada em dentina desmineralizada (KNIGHT et al., 2007) e com isso maior escurecimento também é observada neste substrato alterado (SAYED et al., 2019). Estudos com maior tempo de observação ainda são necessários. Além disso, uma revisão sistemática publicada recentemente (ROBERTS et al., 2020) apontou que as evidências disponíveis não são suficientes para mostrar a vantagem do KI associado ao DFP na redução do escurecimento da dentina tratada, sendo mais estudos necessários. Poucos estudos até o momento avaliaram o efeito do DFP no manchamento, combinado ou não com KI, aplicado imediatamente antes do tratamento restaurador. A aplicação de KI reduziu o manchamento de restaurações de cimento de ionômero de vidro (NGUYEN et al., 2017; ZHAO et al., 2017c), de ionômero de vidro modificado por resina e de ionômero de vidro combinado com restaurações de resina composta (NGUYEN et al., 2017). Nenhum estudo anterior avaliou a coloração da resina composta colocada diretamente na dentina tratada com DFP.

Diante do exposto, esta tese está dividida em três artigos acerca do diamino fluoreto de prata. O primeiro deles, intitulado “Teaching and use of silver diamine fluoride in Pediatric Dentistry: Questionnaire-based cross-sectional analysis of undergraduate Brazilian dental schools” teve como objetivo traçar um panorama do ensino e da utilização do diamino fluoreto de prata nas disciplinas de Odontopediatria das universidades brasileiras de Odontologia. O segundo, intitulado “Bonding of glass-ionomer cement and adhesive systems to silver diamine fluoride-treated dentine: An updated systematic review and meta-analysis “ avaliou sistematicamente a influência da aplicação prévia de DFP na resistencia de união de materiais restauradores diretos à dentina higida ou afetada por cárie. Por fim, o terceiro estudo, intitulado “Evaluation of the use of potassium iodide application on stained demineralized dentin under resin composite following silver diamine fluoride application” avaliou a alteração de cor da dentina e de restaurações de resina composta realizadas após o uso do DFP, com ou sem a aplicação subsequente de iodeto de potássio..

2. ARTIGO 1- TEACHING AND USE OF SILVER DIAMINE FLUORIDE IN PEDIATRIC DENTISTRY: QUESTIONNAIRE-BASED CROSS-SECTIONAL ANALYSIS OF UNDERGRADUATE BRAZILIAN DENTAL SCHOOLS

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Teaching and use of silver diamine fluoride in Pediatric Dentistry: Questionnaire-based cross-sectional analysis of undergraduate Brazilian dental schools

Ensino e uso do diamino fluoreto de prata em Odontopediatria: Análise transversal baseada em questionário em cursos de graduação em odontologia brasileiros

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Teaching and use of silver diamine fluoride in Pediatric Dentistry: Questionnaire-based cross-sectional analysis of undergraduate Brazilian dental schools

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ABSTRACT

This study investigated the teaching and use of silver diamine fluoride (SDF) in Pediatric Dentistry in undergraduate Brazilian dental schools through a questionnaire-based cross-sectional analysis. Two-hundred and thirty-five questionnaires were e-mailed to directors of Pediatric Dentistry of undergraduate Brazilian dental schools. The details of the teaching and use of SDF in clinical practice were asked. Obtained data were analyzed descriptively and using the chi-square test. A total of 149 complete questionnaires were returned (63.4%). Most of schools taught SDF in lectures (73.8%, $p < 0.001$). The majority use SDF in clinical practice (64.4%, $p < 0.001$), but its use is not frequent (11.4%, $p < 0.001$). All dental schools reported that SDF is applied in primary teeth, and few reported its use for permanent teeth (36.4%, $p = 0.01$). SDF has been used mainly for cavitated caries in primary teeth of children aged 0 to 3 years (93.7%, $p < 0.001$), with restricted use in posterior teeth (42.7%, $p < 0.001$). Although SDF is teaching and used in clinical practice in Pediatric Dentistry in most Brazilian undergraduate schools, its use is not frequent. Furthermore, SDF is not considered an option for caries lesions in some dental schools.

Descriptors: Dental Caries. Cariostatic Agents. Pediatric Dentistry. Education, Dental. Survey and Questionnaires.

INTRODUCTION

Silver diamine fluoride (SDF) has been considered one of the most effective treatments for arrest carious lesions in primary teeth.[1] Its use was proposed in Japan[2] in the 70s and later began to be used in Brazil[3] and other countries. It recently came back to prominence mainly after its introduction in the American market in 2014[4], becoming, since then, the focus of numerous scientific investigations. Furthermore, in early 2020, with the global pandemic of Coronavirus 2 of severe acute respiratory syndrome (SARS-CoV-2), the SDF has emerged as a minimally invasive measure with minimal aerosol generation carious lesions treatment [5,6].

Silver diamine fluoride has antibacterial properties, acts on the dental structure's remineralization, and has an inhibitory effect on the organic matrix's degradation [7]. The most common adverse effect related to its use is to make treated carious lesions black [8], forming a layer of silver phosphate on the surface [9]. This clinical observation that SDF causes the compromised tooth structure to darken can be a significant impediment to its use due to aesthetic concerns, especially when anterior teeth are involved [10]. Therefore, the inclusion of SDF as a teaching topic and its use in undergraduate dental schools may be affected.

A recently published study investigated the teaching of silver diamine fluoride in dental schools in the United States and found that it is present in the curriculum of almost 70% of them but is used in clinical practice in less than 50% [11]. Another investigation carried out in residency programs in Pediatric Dentistry, also in American institutions, found that for more than one-half of the respondents, the concern with parental acceptance in the face of the color change associated with arresting of the carious lesion is considered a barrier to its use [12]. The use of SDF was less commonly taught in undergraduate pediatric dentistry in dental schools in the United Kingdom [13]. To the best of our knowledge, there are no investigations on the use of silver diamine fluoride in Brazilian dental schools. Therefore, this study aimed to evaluate the current teaching and use of SDF in Pediatric Dentistry in undergraduate Brazilian dental

schools. The hypothesis tested was that SDF is not taught and not used in most pediatric dentistry disciplines.

MATERIALS AND METHODS

Study Design

This research refers to a questionnaire-based cross-sectional study conducted from September 2019 to April 2020. The project started after review and approval by the Institution's Research Ethics Committee (CAAE 08116619.2.0000.5346) and was designed and conducted according to guidelines of the STROBE statement (Strengthening the reporting of observational studies in epidemiology) [14].

Population

The survey targeted 265 undergraduate dental schools in Brazil, all of them registered with the Federal Council of Dentistry and the Ministry of Education and Culture (MEC). Therefore, a convenience sample was used.

Data Collection

The names and electronic addresses of the heads or other staff members of Pediatric Dentistry were obtained from school websites. A questionnaire about current use and teaching of silver diamine fluoride was developed based on the previous study [15]. An introductory letter, a Free and Informed Consent Form, and a link to the online platform (Google Forms) were sent to a faculty member in charge of each institution's pediatric dentistry teaching.

The questionnaire consisted of 11 questions designed to evaluate the details of the theoretical teaching and clinical use of SDF in the undergraduate pediatric dentistry. The first question asked if the silver diamine fluoride is a theoretical topic of lectures and if it is used in

the clinical practice of pediatric dentistry. When the answer was positive, other specific questions about the use of SDF were presented: frequency and how long it has been used, product concentration, if used in primary teeth and age range, if used in permanent teeth, if used in anterior and/or posterior teeth and for non-cavitated or cavitated lesions, according to the International Caries Detection and Assessment System (ICDAS) considering each type of teeth (primary or permanent).

The questionnaires were sent out again up to five times, with seven days interval among submissions in case of no response. After this period, a new attempt was made for another teacher from the same institution. If more than one questionnaire returned from the same institution, the first questionnaire received was considered.

Data Analysis

The data obtained were summarized using descriptive statistics (percentages) and the chi-square test to compare the proportions obtained. The results were analyzed using the Minitab Express statistical program (Minitab, Inc, State College, PA, USA).

RESULTS

A flow diagram illustrates the sending and receiving of questionnaires (Figure 1). A total of 265 institutions were considered as potential participants. Of these, 20 were excluded from the study for not having started the discipline of Pediatric Dentistry. Also, 10 institutions could not be considered due to the impossibility of contact. Questionnaires were sent to 235 dental schools. A total of 149 dental schools returned the completed questionnaires (overall response rate of 63.4%).

The number of questionnaires answered by Brazilian geographic macro-regions and public or private dental schools is described in Table 1. The majority (78%) of the schools are

private educational institutions, and 60.8% of these private schools returned the completed questionnaire. Fifty-one public educational institutions were consulted, and 72.5% participated in the study. All Brazilian geographic macro-regions were represented in the present study. Southeast and Central-West macro-regions showed higher representation (84.4% and 72.2%, respectively).

In most of the responding schools, the silver diamine fluoride is included as a topic in formal lectures (73.8%, $p<0.001$) and is used in the clinical practice of pediatric dentistry (64.4%, $p<0.001$). The general obtained data are described in Table 2.

Regarding the frequency of use, most schools reported using the SDF rarely (29.5%) or sometimes (27.5%), and in 11.4% of schools, SDF is used frequently ($p<0.001$). It has been in use for less than 5 years (46.8%), although in 37.5 % using it for more than 10 years in the discipline's clinical practice. SDF in a concentration of 30% (52%, $p=0.01$) is used in most schools, despite the concentrations of 38% and 10% or 12%. It is essential to consider that some respondents chose more than one option.

The SDF is used in all institutions to treat carious lesions in primary teeth, but only 36.4% of schools reported its use in permanent teeth ($p=0.01$). For primary teeth, it is used for both anterior and posterior teeth (53.1% of responses), although in some institutions, the use is restricted to posterior teeth (42.7% of responses, $p<0.001$). The SDF is mostly used in children aged 0 to 3 years (93.7%, $p<0.001$), but the application in children aged 5 to 10 years was also reported by most schools (63.5%). Regarding the type of lesion, non-cavitated enamel lesions (ICDAS 1 and 2) have been treated with SDF (33%), even if less frequently than cavitated lesions, both in enamel (ICDAS 3, 63.5%) and dentin (ICDAS 5 and 6, 63.5%). For permanent teeth, it is used almost exclusively in posterior teeth (88.5%, $p< 0.001$) in enamel cavitated lesions (ICDAS 3, 57.1%), non-cavitated lesions (ICDAS 1 and 2, 42.8%), and even in dentin

cavitated lesions (ICDAS 5 and 6, 40%). Tables 3 present the specific data about the use in primary and permanent teeth.

DISCUSSION

Silver diamine fluoride has been used in Brazil since the 1980s; however, recently, it has aroused greater interest and perhaps greater use, as it is a non-invasive technique for caries treatment [1,16] and due to its current availability in the American market [4]. Besides that, the SARS-CoV2 pandemic impact on dentistry requires evidence-based protocols on children's dental care, including those with no or minimum aerosol generation, as the use of SDF [5,6]. This is the first study to investigate the teaching and use of SDF in Brazilian undergraduate dental schools. The overall response rate (63.4%) may be considered satisfactory because of the significant number of dental schools in Brazil; in this study, 235 institutions were contacted, and 149 answered the survey. Also, the obtained response rate is even higher than that related in other Brazilian surveys based on questionnaires [17-19].

This study demonstrates that SDF is a topic of theoretical lectures and is used in the clinical practice of the Pediatric Dentistry of most Brazilian dental schools, then the null hypothesis could be rejected. These findings contrast with the data obtained in American dental schools[11] and from a study carried out in dental schools in the United Kingdom [13]. In the United Kingdom, only one institution reported teaching the technique of silver diamine fluoride. Despite being part of the majority curriculum in American institutions, it is used in clinical practice in less than 50%. Although SDF has been available for more than four decades in some countries like Brazil, only in 2014, the SDF received FDA (Food and Drug Administration) approval for commercialization in the American market [4]. In the United Kingdom, currently, the use of SDF would be on an off-license basis [13]. These may explain the differences observed in SDF use in Brazilian, American, and European institutions. Besides, the great concern with unfavorable aesthetics resulting from SDF use may also explain its non-use.

Silver diamine fluoride has been considered the most effective non-invasive treatment for arrest carious lesions in primary teeth[1]. SDF application is advised for cavitated lesions [20,21], especially with dentinal involvement [22]. In all Brazilian institutions that reported using SDF, use it on primary teeth, especially in children aged 0 to 3 years. The use of SDF is being recommended for the management of early childhood caries [21], and it can prevent or delay surgical intervention until 3 years of age, which makes it a potentially attractive therapy in this very young pediatric population [23]. Despite this, most undergraduate dental schools have also considered the application in children aged 5 to 10 years.

The obtained data pointed out that in most Brazilian dental schools, the SDF is an option for treating cavitated lesions in primary teeth, both in enamel (ICDAS 3) as in dentin (ICDAS 5 and 6). On the other hand, few schools consider its use to treat incipient caries lesions (ICDAS 1 and 2). Unlike what happens for cavitated lesions, there is still no strong evidence to demonstrate SDF's superiority over other treatments for non-cavitated lesions. The recommendation, so far, has been to prioritize the application of fluoride varnishes or sealants [20].

In contrast to the widespread use of silver diamine fluoride for caries arrest in primary teeth, it is not commonly used in permanent teeth in most Brazilian institutions, probably due to the greater aesthetic demand for permanent teeth. Also, the SDF has its main indication for the treatment of early childhood caries, children with no cooperative behavior, that may be considered traditional restorative treatment barriers [24]. In a non-restorative treatment guideline, the application of SDF is recommended for cavitated lesions in primary and permanent teeth; however, it is considered a conditional recommendation for permanent teeth. There is no substantial evidence available to inform its effectiveness on these teeth [20]. It is noteworthy, however, that the literature shows that the SDF is an alternative treatment option for incipient caries in occlusal surfaces of permanent first molars [25,26] and initial and moderate caries (ICDAS

1, 2, and 3) in proximal surfaces of permanent teeth [27]. According to the present results, the use in cavitated enamel lesions was similar to non-cavitated and even cavitated lesion in dentin.

The present study also investigated the use of SDF in anterior or posterior teeth. Most of the respondent schools use SDF in anterior and posterior primary teeth; however, in many institutions (42.7%), its use is restricted to posterior teeth. This finding is probably due to the potential for darkening the teeth treated with SDF [8]. The black staining, a frequent clinical observation following the SDF application, seems to be more acceptable by parents in posterior teeth than in anterior teeth [10]. It is interesting to note that according to a recently published scoping review, in general, the staining caused by SDF did not interfere in the parental acceptability for the treatment. However, it is one of the professionals' concerns and possible impacts on its use [28]. As expected, in almost all institutions, the SDF use in permanent dentition is exclusive to posterior teeth.

Regarding SDF concentrations, products in lower concentrations (10% and 12%) and higher concentrations (30% and 38%) are available in Brazil [1]. Most consulted schools answered using a concentration of 30%. Clinical trials demonstrate that products with the highest concentrations are more effective in arrest caries lesions [29,30], and SDF in a 38% concentration is the most recommended [20]. This is the most used concentration worldwide, but it is used in only a small percentage of Brazilian dental schools. It can be explained by only one product with this concentration (Riva Star, SDI, Victoria, Australia) is more recently available in the Brazilian market. However, clinical studies that evaluated the concentration of 30% guarantee its effectiveness [31-33].

This study also investigated how long the SDF has been used in pediatric dentistry in Brazilian dental schools. Although SDF has been used in Brazil for a long time, almost half of the respondent schools have reported using the silver diamine fluoride for less than five years. The recent interest by the scientific community may have contributed to it. It is also important

to note that, although most Brazilian institutions reported the use of SDF, its use is not frequent. It may be related to the restricted indication for children under 3 years old and in posterior teeth. Besides, there may still be fear of its use due to concern about accepting the color change caused by SDF by parents or guardians, a finding of a previous study carried out in American Pediatric Dentistry Training Programs [12]. Also, it is essential to consider that, at the moment of this research, in some institutions, SDF was not yet considered a treatment option for caries lesions. We can speculate that the SARS-CoV2 pandemic has the potential to highlight techniques that do not generate aerosol [5,6]. Silver diamine fluoride is an excellent alternative, and dental schools that have not yet used it should now consider it as a treatment option for caries lesions in Pediatric Dentistry.

Considering that the SDF has been recognized as an effective non-invasive treatment for caries lesions, knowledge about its use in undergraduate education is essential, especially in Pediatric Dentistry. Thus, the present study results show that the SDF has been considered a treatment option, especially for arresting cavitated carious lesions in primary teeth in children from 0 to 3 years old, as attested by most Brazilian dental schools. However, despite all available scientific evidence about silver diamine fluoride effectiveness, there are still schools that use it rarely or not at all. It is interesting to observe that in previous study[12] in American residency programs in Pediatric Dentistry, only 26% of respondents reported using SDF. Still, the publication of this 2015 study's update[15] now shows that 100% reported its utilization in 2020. It can also highlight the importance of this type of survey to guide and accompany teaching in Pediatric Dentistry. This study encourages Brazilian dental schools to reinforce SDF use in clinical practice as it is a well-established and successful technique for arrest carious lesions, especially in primary teeth.

CONCLUSIONS

Based on this questionnaire-based cross-sectional analysis, silver diamine fluoride has been taught and used in Pediatric Dentistry of most undergraduate Brazilian dental schools, but its use is not frequent. SDF is mainly used for early childhood caries and cavitated lesions in the posterior primary teeth.

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RESUMO

Este estudo investigou o ensino e a utilização do diamino fluoreto de prata (DFP) em Odontopediatria em cursos de graduação em odontologia brasileiros por meio de uma análise transversal baseada em questionário. Duzentos e trinta e cinco questionários foram enviados por e-mail a professores responsáveis pela disciplina de Odontopediatria de cursos de odontologia brasileiras. Os detalhes do ensino e uso de DFP na prática clínica foram solicitados. Os dados obtidos foram analisados descritivamente e por meio do teste do qui-quadrado. Um total de 149 questionários completos foram devolvidos (63,4%). A maioria das escolas ensina sobre o DFP em aulas teóricas (73,8%, p <0,001). A maioria usa o DFP na prática clínica (64,4%, p <0,001), mas seu uso é pouco frequente (11,4%, p <0,001). Todas as escolas de odontologia relataram que o DFP é aplicado em dentes decíduos, e poucas relataram seu uso em dentes permanentes (36,4%, p = 0,01). O DFP tem sido usado principalmente em lesões de cárie cavitadas em dentes decíduos de crianças de 0 a 3 anos (93,7%, p <0,001), com uso restrito aos dentes posteriores (42,7%, p <0,001). Embora o DFP seja tópico de ensino e utilizado na prática clínica em Odontopediatria na maioria das escolas de graduação brasileiras, seu uso é pouco frequente. Além disso, o DFP não é considerado uma opção para lesões de cárie em algumas escolas de odontologia.

Descritores: Cariostáticos. Ensino Odontológico. Odontopediatria. Estudantes de Odontologia.

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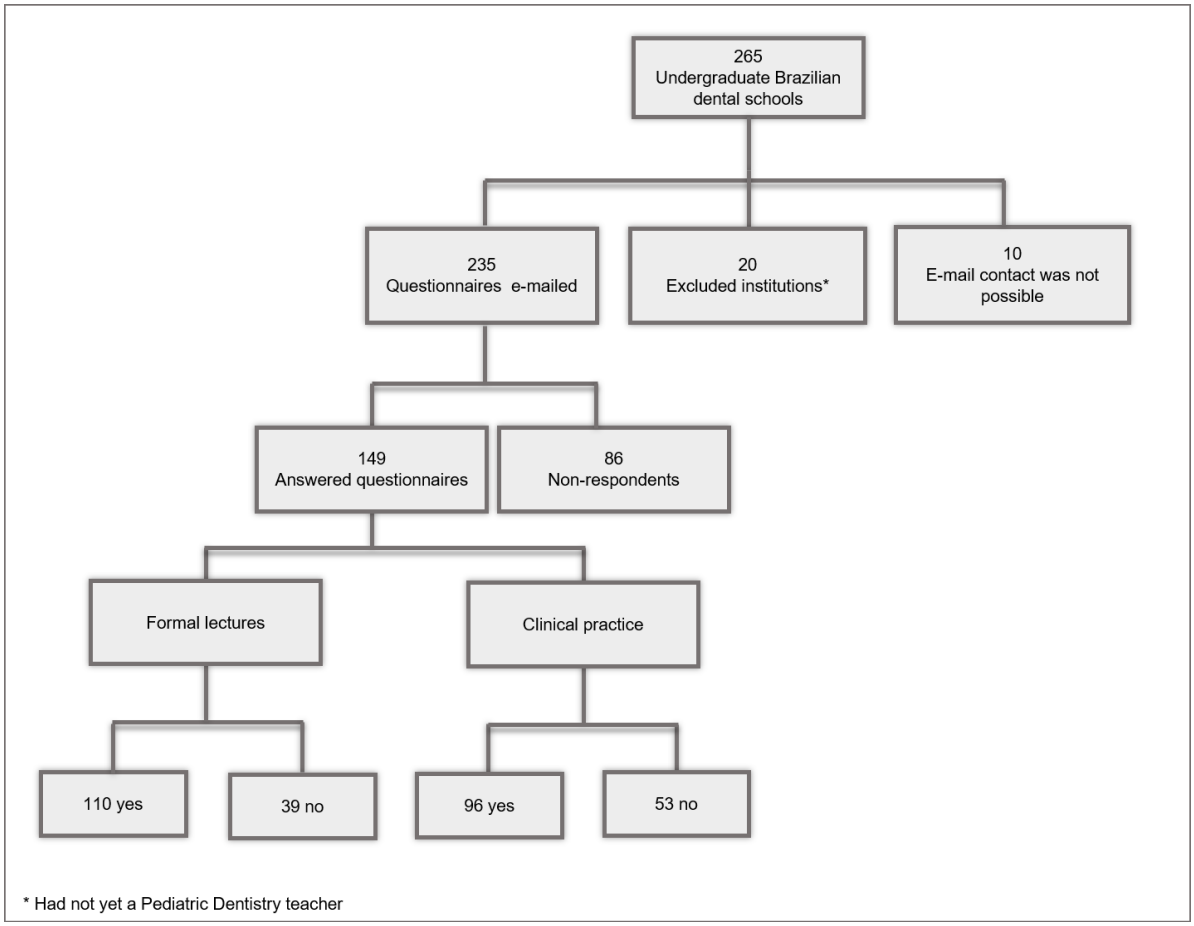

Figure 1. Flowchart for the application of questionnaires in the Pediatric Dentistry disciplines of undergraduate dentistry courses in Brazil.

Table 1. Type and geographic region of undergraduate courses participating in the research.

	Sent e-mails N	**Answered Questionnaires N (%)**
Type of the Institution		
Public	51	37 (72.5)
Private	184	112 (60.8)
Country Region		
North	21	11(52.3)
Northeast	62	33 (53.2)
Central-West	18	13(72.2)
Southeast	89	54 (60.6)
South	45	38 (84.4)
Total	235	149 (100)

Table 2. Results regarding general data about the use of silver diamine fluoride presented in the survey.

Questions	**N(%)***
How often is the SDF are use?	
Frequently	11 (11.4)[#]
Sometimes	41 (27.5)
Rarely	44 (29.5)
How long SDF has it been used by the institution?	
Less than 5 years	45 (46.8)
From 5 to 10 years	15 (15.6)[#]
More than 10 years	36 (37.5)
What product concentration is used?	
10 or 12%	33 (34)
30%	50 (52)[#]
38%	27 (28)
Do not know	5 (5.2)
Is it used on primary teeth?	
Yes	96 (100)[#]
No	0
Is it used on permanent teeth?	
Yes	35 (36.4)
No	61 (63.5)[$]

* Numbers (percentage) marked with superscript symbols show statistically significant differences from the others.
[#] $p<0.001$
[$] $p=0.01$

Table 3. Results regarding specific data about the use of silver diamine fluoride in primary and permanent teeth presented in the survey.

Questions	**N(%)***
Primary teeth**	
What age group is it used?	
0 to 3 years	90 (93.7)[#]
5 to 10 years	61 (63.5)
Over 10 years	14 (14.5)
Which teeth are treated with SDF?	
Anterior	4 (4.1)[#]
Posterior	41 (42.7)
Both	51 (53.1)
Which lesions are treated with SDF?	
Enamel lesions, without cavity (ICDAS 1 and 2)	31 (33)[#]
Enamel cavitated lesions (ICDAS 3)	61 (63.5)
Dentin cavitated lesions (ICDAS 5 or 6)	61 (65.5)
Permanent teeth***	
What types of teeth are treated with SDF?	
Anterior	0
Posterior	31 (88.5)[#]
Both	4 (11.4)
What type of lesions are treated with SDF?	
Enamel lesions, without cavity (ICDAS 1 and 2)	15 (42.8)
Enamel cavitated lesions (ICDAS 3)	20 (57.1)
Dentin cavitated lesions (ICDAS 5 or 6)	14 (40)

* Numbers (percentage) marked with symbols show statistically significant differences from the others. ** N= 96 ***N=35 [#]p<0.001

3. ARTIGO 2- BONDING OF GLASS-IONOMER CEMENT AND ADHESIVE SYSTEMS TO SILVER DIAMINE FLUORIDE-TREATED DENTINE: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS

Este artigo foi submetido ao periódico The Journal of Adhesive Dentistry; ISSN: 1757-9988; Fator de impacto = 1.311; Qualis A2. O artigo está de acordo com as normas deste periódico, que estão descritas no ANEXO B.

Article type: Systematic review

Bonding of glass-ionomer cement and adhesive systems to silver diamine fluoride-treated dentine: An updated systematic review and meta-analysis

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Bonding of glass-ionomer cement and adhesive systems to silver diamine fluoride-treated dentine: An updated systematic review and meta-analysis

Abstract

Purpose: To evaluated through a systematic review and meta-analysis the bonding performance of adhesive materials to silver diamine fluoride (SDF)- treated dentine.

Materials and Methods: Studies located from PubMed, Web of Science, LILACS, and Scopus up to September 2020, comparing the bond strength of adhesive systems (AS) or glass ionomer cement (GIC) to SDF treated and untreated (control) dentine were included. Mean differences were estimated separately by material, and dentine condition (sound or caries-affected), with a random-effect model, at a 5% significance level.

Results: Twenty-two studies, including 11 new studies, met eligibility criteria, and 21 studies were considered in the meta-analyses. SDF dentin pretreatment did not influence the bonding of GIC (Z= 0.53; p= 0.60), independently of dentine condition. SDF treatment significantly impair the bonding of AS (Z= 2.43; p= 0.01). Rinsing step after SDF eliminate this effect in sound dentine (Z= 1.82; p= 0.07) and increase the bonding to caries-affected dentine (Z= 2.14; p= 0.03).

Conclusion: The SDF pretreatment does not influence the bond strength of GIC. Rinsing step after SDF application can improve the bonding of AS to caries-affected dentine.

Keywords: Bond strength, adhesion, glass ionomer cement, adhesive system, silver diamine fluoride

Introduction

Silver diamine fluoride (SDF) has been considered the most effective non-invasive treatment for carious lesions, especially for primary teeth.[5] SDF has bactericidal properties, inhibits demineralization, and promotes the remineralization of demineralized dentine.[56] Also, it inhibited collagenases (matrix metalloproteinases and cysteine cathepsins) and protected dentine collagen from destruction.[30,31]

Due to these properties, SDF has a potential application as an adjunct to restorative treatment to prevent recurrent caries lesions.[26,53] In vitro studies show that SDF dentine treatment previously to restorations features higher resistance to the development of new lesions when submitted to the cariogenic challenge.[32,36,57] However, a silver phosphate layer was formed on the SDF treated dentine surface,[40] and silver particles extend into the dentinal tubules, causing their total or partial obstruction,[22] which could impair the adhesion of restorative materials.

A previous systematic review and meta-analysis[11] showed that the SDF pretreatment does not negatively influence the bond strength of glass ionomer cement to dentine but can impair the adhesive systems' bond strength. The rinsing step after the SDF application eliminates this adverse effect. However, few studies considered caries-affected dentine at the time of the review, and a separate meta-analysis with these data could not be performed. Worst results can be expected for caries-affected dentine as chemical and morphological differences, such as a lower mineral content[1] and increased porosity of intertubular dentine,[33] jeopardizing the bonding.[18] Moreover, it is essential to consider that higher levels of silver precipitated were formed on the demineralized compared with sound dentine.[22]

The interest in using the SDF as dentine pretreatment has increased since the publication of the systematic review,[11] and several studies were published, including evaluating this effect on caries-affected dentine,[3,9,19,34,46,49,50] a relevant substrate in daily clinical practice, even if

short-term evaluations. Some authors found that previous SDF application in caries-affected dentine does not impair[19,50] or even improve the bond strength values.[9,46] However, other studies showed a significant reduction in bonding.[3,26] Therefore, this study aimed to update the systematic review and meta-analysis on the influence of silver diamine fluoride on direct restorative materials' bonding performance to sound and caries-affected treated dentine. The null hypothesis tested was that the SDF pretreatment does not influence the bond strength of glass ionomer cement and adhesive systems regardless of the dentine condition, sound, or caries-affected.

Materials and Methods

This systematic review was written following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement.[38] The literature approach and search strategy were developed based on the following PICO (participant/problem, intervention, comparator, and outcome) question: the previous application of silver diamine fluoride influences the bond strength of direct restorative materials to sound and caries-affected dentine?; where direct restorative materials - glass ionomer cement and adhesive systems were the participant problem, prior silver diamine fluoride application was the intervention, and no previous application was the comparator, and the bond strength was the outcome.

Search Strategy

A comprehensive literature search was undertaken through the electronic databases PubMed/MEDLINE, ISI Web of Science, Scopus, and LILACS to identify literature up to September 2020, with no language or publication year limits.

The subject search used a combination of controlled vocabulary and text words based on the search strategy developed for the PubMed/MEDLINE database as follow: ((((((((((bond strength) OR microtensile) OR micro shear) OR tensile) OR Tensile

Strength[MeSH Terms]) OR tensile strength) OR shear) OR shear strength) OR Shear Strength[MeSH Terms])) AND (composite resins[MeSH Terms]) OR composite resins) OR composite resin*) OR resin composite* OR Adhesives[MeSH Terms] OR adhesive* OR adhesion OR adhesive system* OR Dental Bonding[MeSH Terms] OR dental bonding OR Dentin-Bonding Agents[MeSH Terms] OR dentin bonding agent* OR total-etch adhesive* OR total-etch adhesive system* OR total-etch OR total-etching OR conventional adhesive OR etch-and-rinse adhesive* OR self-etch adhesive* OR self-etch adhesive system* OR self-etch* OR self-etching primer* OR all-in-one adhesive* OR one-bottle adhesive* OR universal adhesive* OR glass ionomer cements[MeSH Terms] OR glass ionomer cements OR glass ionomer cement OR glass polyalkenoate cement* OR resin-modified glass ionomer cement* OR highly viscous glass ionomer cement* OR high viscosity glass ionomer cement AND (((((silver fluoride) OR silver diamine fluoride) OR SDF) OR diamine fluoride). For ISI Web of Science, LILACS and Scopus the following search terms were used: (Silver Diamine Fluoride) OR (Silver Fluoride) AND (Bond Strength).

Study Selection

Screening of titles and abstracts of all studies were performed to select studies according to the inclusion criteria: in vitro studies that evaluated the bond strength of direct restorative material - glass ionomer cement and adhesive systems/resin composite to previously SDF treated dentine. The full-text of potentially eligible studies were assessed. Those with no control group (dentine without prior application of silver diamine fluoride), had assessed root dentine or used different application protocols of restorative material between the experimental and control groups were excluded. The reference lists of all included studies were manually screened to retrieve all relevant papers. The study selection was done by two independent

reviewers (kappa = 0.90), and any disagreement regarding the eligibility was solved through discussion and consensus by a third reviewer.

Data extraction

The data were extracted according to a predefined protocol using a form in Microsoft Office Excel 2013 (Microsoft Corporation, Redmond, WA, USA). For each paper, the following data were systematically extracted: publication year, country, number of teeth per group, type of teeth, silver diamine fluoride and restorative material used, application protocol, bond strength test, dentine condition (sound or caries-affected), type of carious lesion (natural or artificial), bond strength mean values (in MPa) and standard deviations (SD). The authors were contacted via e-mail (at least twice) to retrieve the bond strength values that did not present as mean and standard deviation. If the authors did not provide the values, the study was not included in the systematic review.

Risk of bias assessment

The risk of bias was based on and adapted from a previous study.[44] The considered domains were: random sequence generation of the teeth for experimental groups, sample size calculation, the same number of teeth per group, failure mode evaluation, silver diamine fluoride and restorative materials applied following manufacturers' instructions, materials and testing procedures performed by a single operator, specimens tested by a blinded operator. If the parameter was described in the text, the study received a "yes," otherwise, it had a "no" or "unclear" (no information or uncertainty over the potential for bias). The risk of bias was classified according to the sum of "yes" received as follows: 1–3 = high,4–5 = medium, 6–8 = low risk of bias. If needed, authors were contacted via e-mail (at least two attempts were made) for missing or unclear information.

Data analysis

Through a random-effects meta-analysis, the pooled-effect estimates were obtained by comparing the standardized mean difference between the bond strength values of SDF treated dentine and control groups, separately for each considered restorative material. Subgroup analyses were carried out according to the SDF application protocol (including or no the rinsing step after the SDF application time) and dentin condition (sound or caries-affected), $p \leq 0.05$ was considered statistically significant (Z-test). For studies that evaluated more than one adhesive system, it was necessary to combine the obtained bond strength values (regardless of the etching strategy) into one mean and one standard deviation using a formula suggested by Cochrane Statistical Guidelines.[17] Only the immediate values of bond strength were considered for analysis. Forest charts were created to illustrate the meta-analysis. Statistical heterogeneity of the treatment effect among studies was assessed using the Cochran Q test and inconsistency I^2, with a p-value of 0.1.[17] All analyses were performed using Review Manager Software 5.3 (The Cochrane Collaboration; Copenhagen, Denmark).

Results

Search and selection

The search strategy identified 1630 potentially eligible studies in all databases. Duplicates were removed, and 1500 studies remained to the inclusion criteria. After screening titles and abstracts, 1478 studies were excluded. Whit this, 22 studies remained after the full-text assessment. For the meta-analysis, 21 studies were included because one of the studies[54] did not present means and standard-deviation, and the missing data were not obtained from the authors through e-mail. A flowchart of the study selection process according to the PRISMA Statement[38] and the reasons for exclusions is shown in Figure 1.

Descriptive analysis

Table 1 and Table 2 show the descriptive data of the included studies, separately by restorative material, glass ionomer cement, and adhesive systems, respectively. Studies were published between 1993 and 2020, all in English. Almost all of the included studies are from the last eight years, except two[23,54] evaluating glass ionomer cement bonding.

For glass ionomer cement, twelve studies were included.[3,10,15,19,23,25,34,42,49,52,55] The studies come from mainly 3 countries/regions – Japan, India, and Hong Kong. SDF concentration of 30% or 38% associated with potassium iodide solution were evaluated. The majority of the studies evaluated glass ionomer cement modified by resin or high viscosity; only three used conventional glass ionomer cement.[3,23,52] Five studies evaluated the bonding of glass ionomer cement to sound dentine,[10,15,23,34] four considered caries-affect dentine,[34,42,49,55] and three evaluated the two substrate conditions.[3,19,52] Of the studies that assessed caries-affect dentin, most used artificial lesions and only one stuy[42] used natural lesions. The majority assessed permanent teeth; only two studies used primary molars.[42,49] Shear bond strength was the most used mechanical test, followed by the microtensile bonding test.

For adhesive systems, eleven studies were included.[9,24-26,28,29,43,45,46,50,53] The studies come mainly from USA. The majority of studies use the SDF concentration of 30% or 38% associated with the potassium iodide solution. Only two studies[43,46] evaluated both SDF 38% and SDF 12%, and one study[24] assessed SDF 38% and 3.8%; therefore, data referring to a concentration of 12% and 3.8% were not considered. Sound dentine was the bonding substrate considered in most studies; only four studies[9,26,46,50] evaluated the bond strength to caries-affected dentine. Of the studies that assessed caries-affect dentin, most used artificial lesions and only one study9 used natural lesions. Only one study considered the bonding to primary dentine.[53] The microtensile was mechanical testing more used.

Meta-analysis

Glass ionomer cement

Figure 2 shows the results for the meta-analysis considering glass ionomer cement. No significant difference was found between control and SDF groups (Z=0.53; p = 0.60) in the overall meta-analysis, with moderate heterogeneity (X^2 test; p = 0.04; I^2 = 41 %). The SDF pretreatment do not affect the bond strength to sound dentine, with (Z=0.93; p=0.35) or without the rinsing step (Z=1.11; p=0.27). The data show heterogeneity for rinsing subgroup (X^2 test; p = 0.03; I^2 = 65 %) and no heterogeneity for subgroup without step of rinsing (X^2 test; p = 0.43; I^2 = 0 %). Similarly, the pretreatment with SDF don't jeopardize the bond strength to caries-affected dentine, with (Z=0.99, p=0.32) or without the step of rising (Z=0.92, p=0.36). The data show moderate heterogeneity for rinsing subgroup (X^2 test; p = 0.16; I^2 = 39%) and no heterogeneity for subgroup without step of rinsing (X^2 test; p = 0.82; I^2 = 0 %).

Adhesive systems

Figure 3 shows the results of meta-analysis for adhesive systems. SDF applied previously to adhesive system significantly impair the bond strength to dentine in overall meta-analysis (Z = 2.43; p =0.01) and in sound dentine subgroup without rinsing step (Z= 2.93; p<0.01). The data were heterogeneous (X^2 test; p < 0.01; I^2 = 98% and p < 0.01; I^2 = 95%). The rinsing step eliminated the negative effect of SDF application in sound dentine (Z= 1.82; p=0.07) and increased the bonding of adhesives systems to caries-affected dentine (Z= 2.14, p=0.03). Data with heterogeneity in the two analyses (X^2 test; p<0.01; I^2=97%; X^2 test; p= 0.1; I^2= 72%).

Risk of bias

The results of the assessment of the risk of bias are described in Table 3. One study cannot have its risk of bias assessed,[50] as it was not obtained in the full version, and some

domains could not be evaluated. The majority of the studies included presented medium (10 studies) or high (8 studies) risk of bias. The parameters that most often received “no” were: the description of sample size calculation, a single operator during the specimen preparation, and the blinded operator during the tests.

Discussion

The present study updates a previous systematic review and meta-analysis on the influence of silver diamine fluoride application on dentine bond strength of glass ionomer cement and adhesive systems.[11] The first review[11] included 11 studies, the majority of them evaluating the previous application of SDF in sound dentine, so an independent analysis with data of caries-affected dentine could not be investigated. This updated systematic review, conducted by the same research group, included 22 studies; 10 studies were eligible for this review (6 new studies), evaluating the caries-affected dentine substrate, a more relevant substrate in the daily clinical practice. Another systematic review was recently published, without, however, including the total of studies considered in this review.[20]

According to the previous systematic review,[11] the effect of SDF application on the dentin bonding was material-dependent, as it does not influence the bonding of glass ionomer cement but can impair the bond strength of adhesive systems if SDF was not rinsed after application. Therefore, new subgroups meta-analyses were performed considering studies that assessed the SDF effect in caries-affected dentine. As in the previous review, the SDF pretreatment in caries-affected dentine does not impair the glass ionomer cement's bonding. Likewise, the SDF application, followed by rinsing, does not jeopardize adhesive systems' bond strength. Therefore, considering the obtained results, the hypothesis of this updated review was partially accepted.

The present findings show that regardless of dentine condition (sound or caries-affected), the bonding of glass ionomer cement was not affected by SDF pretreatment. It could

be explained by the bonding mechanism of glass ionomer cement based on a chemical reaction between polyacrylic acid from glass ionomer and calcium ions (from hydroxyapatite mainly).[14] Besides, the SDF protocol (with or without the rinsing step) did not influence dentine's bond strength in both substrate conditions. However, even in studies that did not carry out the rinsing step immediately after the SDF, a conditioner, such as polyacrylic acid,[3,10,19,25] was applied before restoration. Thus, the rinsing step or the application of polyacrylic acid can be necessary for proper adhesion of glass ionomer cement to SDF-treated dentine to eliminate the silver precipitate excess and increase the ion exchange for an acid-base reaction.

In contrast to the glass ionomer cement results, the adhesive systems bonding to dentine could be impaired by SDF pretreatment. The silver precipitate formed in the dentin surface and dentin tubules could be responsible for adversely affect the bonding of the adhesive system, as the bonding mechanism of adhesives is based on micromechanical retention and hybrid layer formation in dentine.[4,16] As in the first review, this update considered the adhesive systems in the same group, regardless of the etching strategy (etch-and-rinse or self-etch), as in other reviews,[2,7,41] considering that the main goal was to evaluate the influence of SDF on dentin bonding.

The negative effect of SDF in adhesive systems bonding was eliminated when the rinsing step after the application time is carried out, even in caries-affected dentine. The worst result was expected in caries-affected dentine due to the chemical and morphological differences,[1,33] and higher silver precipitated levels formed on demineralized dentine,[22] but this was not confirmed in this systematic review. On the contrary, the pretreatment with SDF followed by the rinsing step could increase adhesive systems' bonding to caries-affected dentine. Only one study[26] assessed the previous SDF application in caries-affected dentine without the rinsing step, this subgroup analysis cannot be performed. Even so, according to this primary study,[26] the SDF application jeopardizes the dentine bond strength. Immediately after

the SDF application, the rinsing step can eliminate the excess of silver precipitate from peritubular and intertubular dentine,[28] favoring the adhesion. Besides, SDF can remineralize the caries-affected dentin,[56] improving the mechanical properties of this altered substrate. However, this finding is based on only three studies,[9,46,50] so more investigations evaluating the bonding mechanism of adhesive systems to SDF-treated caries-affected dentine are necessary to confirm this result.

The application of SDF to prevent recurrent caries is a new and off-label use; therefore, few studies evaluating its effect on bond strength of restorative materials are available, explaining the number of eligible studies. However, it is essential to note that shortly after the publication of the first systematic review,[11] twice as many articles can be included in this update, demonstrating the growing interest in this use of the SDF. Despite the considerable increase in the number of studies, only one new study evaluating primary teeth was included.[49] Thus, although SDF is most commonly used for arresting caries in primary teeth,[5] few studies assessed the influence of previous SDF application on the bonding of restorative materials in these teeth (two evaluating glass ionomer cement[42,49] and only one considering adhesive system)[53]; thus a separate meta-analysis cannot yet be performed. Considering that bond strength evaluations can measure one specific parameter, controlling the other variables, so more laboratory investigations should be conducted to evaluate the effect of SDF on bonding to primary dentine.

SDF can inhibit matrix metalloproteinases (MMPs), avoiding dentine collagen degradation.[30,31] It is known that the intrinsic degradation (proteolysis) of collagen fibers in dentine by enzymes such as MMPs can compromise the bonding interface, decreasing the bond strength of restorative materials in the long term,[37,39] and the use of MMP inhibitors has been considered an effective strategy to improve the longevity of adhesive restorations.[37,48] However, only one included study evaluated the bond strength of an etch-and-rinse adhesive system to

SDF-treated dentine after 6 months of water storage;[9] therefore, the influence of aging could not be evaluated through a meta-analysis. This study[9] found that previous SDF application on sound dentine restricted the effect of water storage on the bond strength; however, on caries-affected dentine, a significant reduction of bond strength after water storage was shown in the SDF treated group. Therefore, long-term studies are needed to determine the effect of silver diamine fluoride in bond strength after aging.

The present systematic review assessed SDF influence on bonding, mainly in the concentrations of 30% SDF and 38%, as previous studies demonstrated that products with the highest concentrations are more effective in arresting caries lesions.[12,13] Also, only two included studies assessed the 12% SDF.[43,46] Moreover, 9 included studies evaluated the dentine's pretreatment with 38% SDF associated with potassium iodide (KI) before restorations.[10,15,23,25,45,46,49,50,55] The subsequent application of KI is suggested to minimize the inherent disadvantage of using SDF to make treated areas dark.[40] A previous study[57] suggests that the association SDF+KI is not as effective as SDF alone in preventing secondary caries, while another[23] reported that this association was more effective in inhibiting the migration of Streptococcus mutans through dentine than SDF alone. So, there are doubts regarding the effectiveness of SDF with KI for caries prevention.

As found in this systematic review, the high heterogeneity is a common finding in meta-analyses of laboratory studies[6,27,44,47] and may be influenced by the SDF application protocol, restorative material, different methodologies for achieved the caries-affected dentin and bond strength test. Besides, most studies included presented a high or medium risk of bias. Although there is a guideline for conducting and reporting in vitro studies on dental materials,[8] it seems that it has not been commonly used, so this finding in systematic reviews of laboratory studies seems usual.[6,27,47]

This systematic review evaluated the bond strength of glass-ionomer cement and adhesive systems to silver diamine fluoride-treated dentine. The bond strength tests have been commonly used to evaluate restorative materials to predict their performance and the influencing variables - as SDF's previous application. Although the relationship between in vitro studies with the clinical performance is challenging to establish,[51] a material's adhesive ability is an indicator of the restorations' longevity; superior laboratory performance is probably indicative of better clinical performance.[35] Despite this, ideally, the results of in vitro studies should be confirmed by long-term laboratory studies and randomized clinical trials, evaluation not only the effect of SDF pretreatment on bonding but also considering the interface integrity, secondary caries, and staining. At the moment of this review, there is only one randomized clinical trial with 24 months of follow-up, evaluating the prior application of SDF on cavitated dentine caries lesions in primary teeth before atraumatic restorative treatment (ART) approach,[21] showing that SDF not jeopardizing the success rate of the restorations.

The present systematic review pointed out that silver diamine fluoride's prior application does not influence the glass ionomer cement's bond strength to dentine, regardless of sound or caries-affected. On the other hand, the SDF application can impair the bonding of adhesive systems. However, the rinsing step after SDF seems to eliminate this adverse effect in sound dentine and improved the bond strength to caries-affected dentine.

Conclusion

Based on the obtained results of this systematic review and meta-analysis of in vitro studies, it can be concluded that the SDF pretreatment does not jeopardize the bonding of glass ionomer cement to dentine. The same is valid for adhesive systems only if the rinsing step after SDF would be performed, which can even improve the adhesion of this restorative material to caries-affected dentine.

Clinical relevance:

The dentin pretreatment with silver diamine fluoride does not affect the adhesion of glass ionomer cements. If the rinsing step after SDF is not carried out, the bonding of the adhesive systems to dentine may be compromised.

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Table 1. Descriptive data of the included studies - glass ionomer cement

Study	Country	Number of teeth per group	SDF	SDF protocol*	Restorative material	Type of teeth	Dentin condition	Type of carious lesion	Bond strength test**
Braz et al., 2020[3]	Brazil	7	Advantage Arrest[<] (38%SDF)	Rinsed Not rinsed	Fuji II LC[@] Riva Self-Cure[&]	Permanent teeth	Sound and Carious	Artificial (pH- cycling model)	µSBS
François et al., 2020[10]	France	20	Riva Star[&] (38% SDF and KI)	Not rinsed	Equia Forte Fil[@]	Permanent molar	Sound	-	SBS
Gupta et al., 2019[15]	India	8	Riva Star[&] (38% SDF and KI)	Rinsed	Gold Label 2 LC[@]	Permanent molar	Sound	-	SBS
Jiang et al., 2020[19]	Hong Kong	15	Saforide[$$$] (38% SDF)	Not rinse	Ketac-Molar Aplicap [#]	Permanent molar	Sound and Carious	Artificial (microbiologically model)	µTBS
Knight et al., 2006[23]	Australia	10	*** (1.8M SDF and KI)	Not rinsed Rinsed	Fuji VII[@]	Permanent molar	Sound	-	SBS
Koizumi et al., 2016[25]	Japan	10	Riva Star[&] (38% SDF and KI)	Not Rinsed	Riva Bond LC[&]	Permanent molar	Sound	-	µTBS
Ng et al., 2020[34]	USA	10-12	Advantage Arrest[<] (38% SDF)	Not Rinsed	Fuiji IX GP Extra Capsule[@]	Permanent molar	Carious	Artificial (demineralising solution)	SBS
Puwanawiroj et al., 2018[42]	Thailand	40	Saforide[$$$] (38% SDF)	Rinsed	Fuiji IX GP Extra Capsule[@]	Primary molar	Carious	Natural	µTBS
Uchil et al., 2020[49]	India	9	Fagamin[$$$$] (38% SDF) Lugol's solution 10 wt% (KI)[%]	Rinsed	Gold Label Ligth-Cure Universal[@]	Primary molar	Carious	Artificial (microbiologically model)	µTBS
Wang et al., 2016[52]	Hong Kong	4	Saforide[$$] (38% SDF)	Rinsed	Fuji IX[@]	Permanent molar	Sound and carious	Artificial (demineralising solution)	µTBS
Yamaga et al., 1993[54]	Japan	***	Saforide[$] (38% SDF)	Not rinsed	Hy-Bond[#]	Bovine incisor	Sound	-	SBS
Zhao et al., 2019[55]	Hong Kong	20	Riva Star[&] (38% SDF and KI) Saforide[$$$] (38% SDF)	Rinsed Not rinsed	Ketac-Molar[#]	Permanent	Carious	Artificial (demineralising solution)	SBS

SDF protocol: not rinsed or rinsed after the waiting time
[a] Elapsed time between the placement of SDF and restoration
**SBS: shear bond strength; µTBS: microtensile bond strength; µSBS: microshear bond strength.
*** Not informed. [$] Toyo Pharmaceutical Co., Tokyo, Japan. [#] Shofu Inc., Tokyo, Japan. [@] GC Corp., Tokyo, Japan. [#] 3M/ESPE Dental Products,USA
[&] SDI Ltda. Victoria, Australia. [$$] Morita Corporation, Osaka, Japan. [$$$] Bee Brand Medico Dental Co. Ltda., Osaka, Japan [$$$$] Tedequim Company, Córdoba, Argentina [<] Elevate Oral Care, West Palm Beach, FL, USA [%] Nice Chemicals, Kochi, India

Table 2. Descriptive data of the included studies - adhesive systems

Study	Country	Number of teeth per group	Silver Diamine Fluoride (SDF)	SDF protocol*	Restorative material	Type of teeth	Dentin condition	Type of carious lesion	Bond strength test**
Firouzmandi et al., 2020[9]	Iran	12	Ancarie Cariostatic° (30% SDF)	Rinsed	Adper Single Bond 2%	Permanent molar	Sound and Carious	Natural	µSBS
Ko et al., 2020[24]	Hong Kong	16	Saforide$$ (38%SDF) Saforide RC$$ (3.8% SDF)	Rinsed	Clearfil SE Bond#	Permanent molar	Sound	-	µTBS
Koizumi et al., 20016 [25]	Japan	10	Riva Star& (38% SDF and KI)	Not rinsed	Optibond FLˆ Optibond Versaˆ Clearfil Liner Bond#	Permanent molar	Sound	-	µTBS
Kucukylmaz et al., 2016[26]	Turkey	8	Saforide$ (38% SDF)	Not rinsed	Clearfil SE Bond#	Permanent molar	Sound and carious	Artificial (pH- cycling model)	µTBS
Lutgen et al., 2018[28]	USA	10	Advantage Arrest< (38% SDF)	Not rinsed Rinsed	Clearfil SE Bond 2# Scotchbond Universal%	Permanent molar	Sound	-	µSBS
Markham et al., 2020[29]	USA	15	Advantage Arrest< (38% SDF)	Rinsed	Scotchbond Universal% Prime & Bond NT> G-Premio Bond£	Permanent molar	Sound	-	SBS
Quock et al., 2012[43]	USA	7	Saforide$ (38% SDF) Ancarie Cariostatic° (12% SDF)	Rinsed	Peak SE@ Peak LC@	Permanent molar	Sound	-	µTBS
Selvaraj et al., 2016[45]	India	18	Riva Star& (38% SDF and KI)	Rinsed	Adper Single Bond 2% Adper Easy One%	Permanent molar	Sound	-	µSBS
Siqueira et al., 2020[46]	Brazil	5	Riva Star& (38% SDF and KI) Cariestop? (12% SDF)	Rinsed	Clearfil Universal Bond Quick# Scotchbond Universal%	Permanent molar	Carious	Artificial (microbiologically model)	µTBS
Van Duker et al., 2019[50]	USA	10	Advantage Arrest< (38% SDF) Saturated solution of KI	Rinsed	Scotchbond Universal%	Permanent molar	Carious	Artificial (demineralising solution)	µTBS

Wu et al., 2016[53]	USA	12	Saforide[$] (38% SDF)	Rinsed	Prime & Bond NT[>]	Primary molar	Sound	-	µTBS

** SDF protocol: not rinsed or rinsed after the waiting time
[a] Elapsed time between the placement of SDF and restoration
**µTBS: microtensile bond strength; µSBS: microshear bond strength.
[°] Maquira Dental Product, Maringa, PR, Brazil
[$] Toyo Seiyaku Kansei Ltd, Osaka, Japan.
[$$]Bee Brand Medico Dental Co. Ltda., Osaka, Japan
[@] Ultradent, South Jordan, UT, USA.
[&] SDI Ltda. Victoria, Australia.
^ Kerr Corp., Orange, CA, USA
[#] Kuraray Noritake Dental Inc., Tokyo, Japan
[%] 3M ESPE, St Paul, MN, USA.
? Biodinâmica, RJ, Brazil
[<] Elevate Oral Care, West Palm Beach, FL, USA.
[>] Dentsply Caulk, Milford, Del., USA.
£ GC, Tokyo, Japan

Table 3. Risk of bias assessment for each included study

Study	Random sequence	Sample size calculation	Same number of teeth per group	Failure mode evaluation	SDF application protocol according manufactures	Restorative material application protocol according manufactures	Single operator	Blinded operator	Risk of bias
Glass ionomer cement									
Braz et al., 2020[3]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Low
François et al., 2020[10]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Gupta et al., 2019[15]	No	No	Yes	No	Yes	Yes	No	No	High
Jiang et al., 2020[19]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Knight et al., 2006[23]	No	No	No	No	Unclear	Unclear	No	No	High
Koizumi et al., 2016 [25]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Ng et al., 2020[34]	Yes	No	No	No	Yes	Yes	No	No	High
Puwanawiroj et al., 2018[42]	Yes	No	Yes	Yes	Unclear	Unclear	No	No	High
Uchil et al., 2020[49]	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Medium
Wang et al., 2016[52]	Yes	No	Yes	Yes	Yes	Unclear	No	No	Medium
Yamaga et al., 1993[54]	No	No	Yes	Yes	No	No	No	No	High

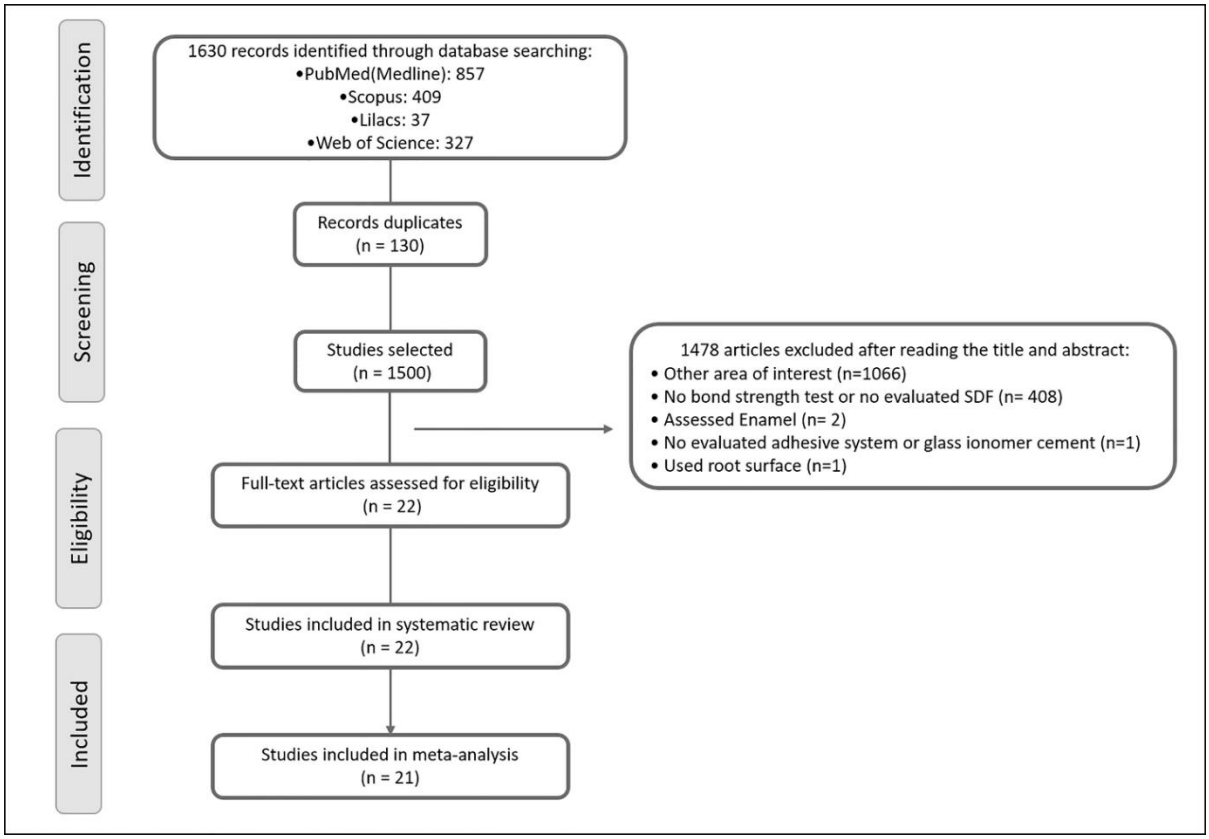
Zhao et al., 2019 [55]	Yes	No	Yes	Yes	Unclear	Unclear	No	No	High
Adhesive systems									
Firouzmandi et al., 2020[9]	Yes	No	Yes	Yes	Unclear	Yes	No	No	Medium
Ko et al., 2020[24]	Yes	No	Yes	Yes	Unclear	Yes	No	No	Medium
Koizumi et al., 20016 [25]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Kucukylmaz et al., 2016[26]	Yes	No	Yes	Yes	Unclear	Unclear	No	No	High
Lutgen et al., 2018[28]	No	No	Yes	Yes	Yes	Yes	No	No	Medium
Markham et al., 2020[29]	No	No	Yes	Yes	Unclear	Yes	No	No	High
Quock et al., 2012[43]	Yes	No	Yes	Yes	No	Yes	No	No	Medium
Selvaraj et al., 2016[45]	Yes	No	Yes	Yes	No	Yes	No	No	Medium
Siqueira et al., 2020[46]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Low
Wu et al., 2016[53]	No	No	Yes	Yes	Unclear	Yes	No	No	High

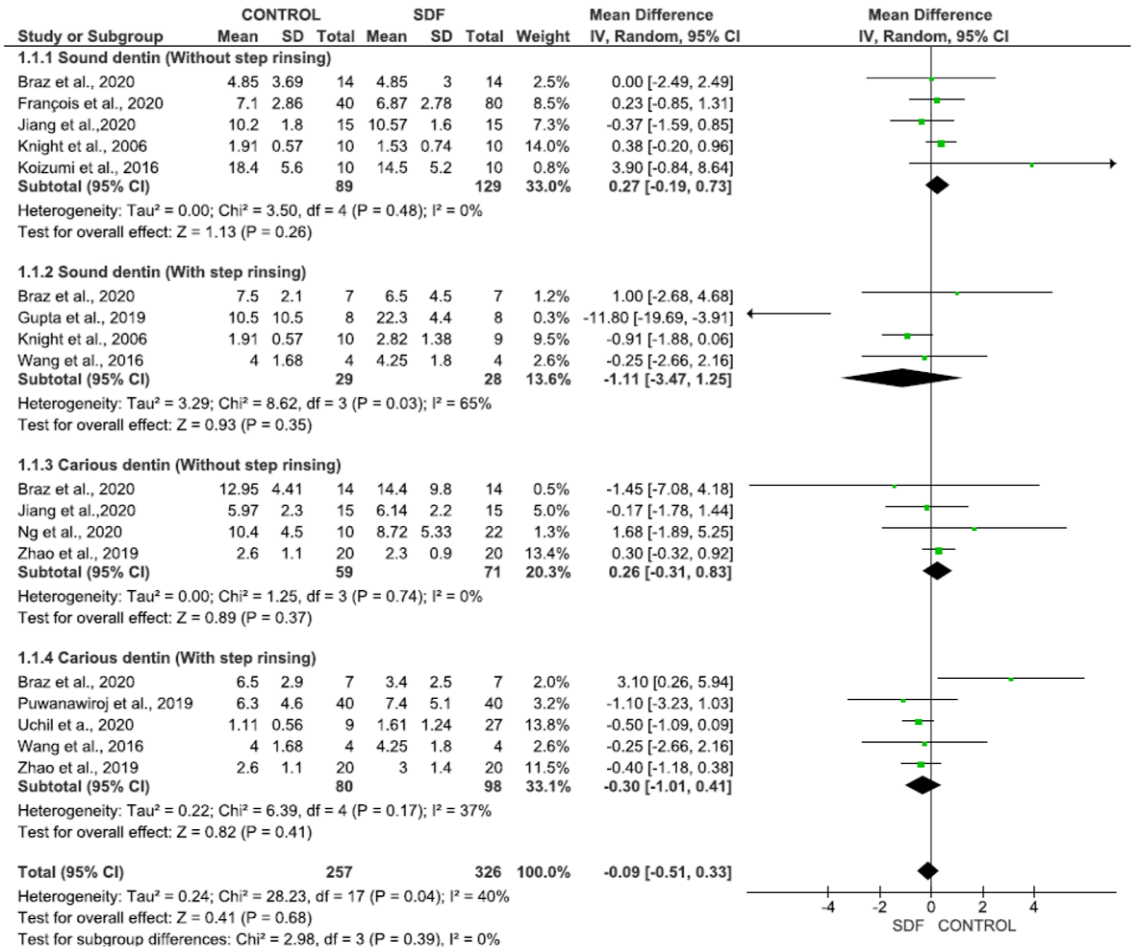
Figures legends

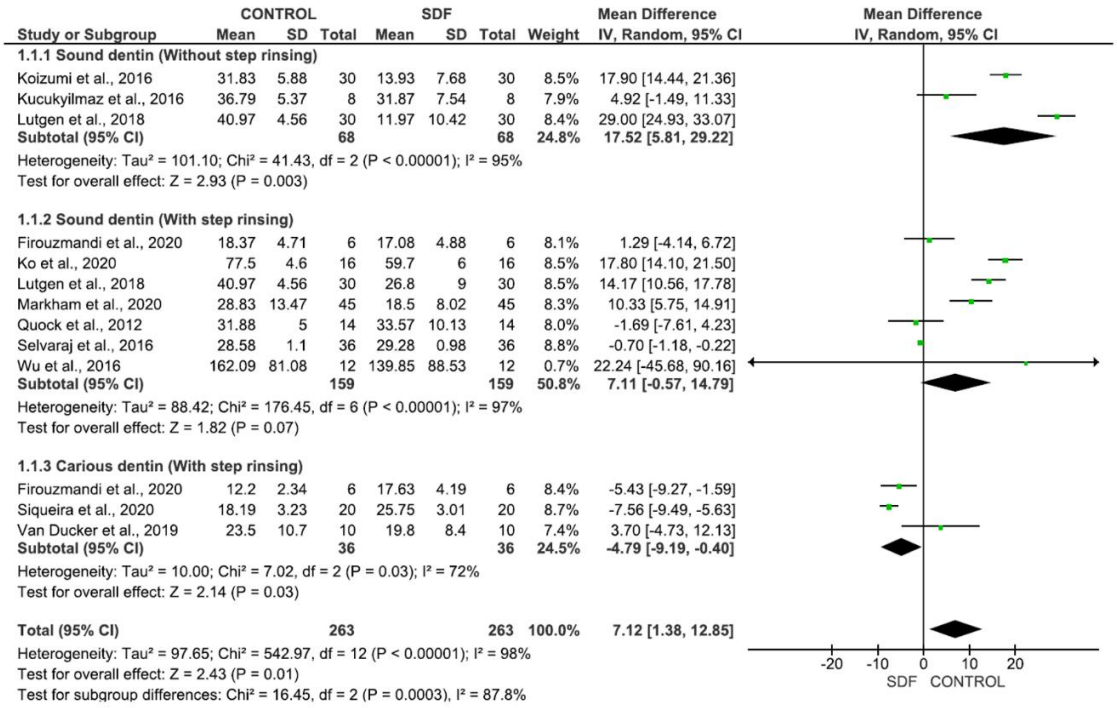
Figure 1. Flowchart diagram of study selection according to the PRISMA statement.

Figure 2. Meta-analysis findings comparing the bond strength of glass ionomer cement to SDF treated (SDF) and untreated (Control) dentine according to SDF protocol (with or without rinsing step) and dentine condition (sound or caries-affected)

Figure 3. Meta-analysis findings comparing the bond strength of adhesive systems to SDF treated (SDF) and untreated (Control) dentine according to SDF protocol (with or without rinsing step) and dentine condition (sound or caries-affected)


Identification
Screening
Eligibility
Included
1630 records identified through database searching:
•PubMed(Medline): 857
•Scopus: 409
•Lilacs: 37
•Web of Science: 327
Records duplicates
(n = 130)
Studies selected
(n = 1500)
1478 articles excluded after reading the title and abstract:
• Other area of interest (n=1066)
• No bond strength test or no evaluated SDF (n= 408)
• Assessed Enamel (n= 2)
• No evaluated adhesive system or glass ionomer cement (n=1)
• Used root surface (n=1)
Full-text articles assessed for eligibility
(n = 22)
Studies included in systematic review
(n = 22)
Studies included in meta-analysis
(n = 21)


CONTROL
SDF
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.1.1 Sound dentin (Without step rinsing)
Braz et al., 2020 4.85 3.69 14 4.85 3 14 2.5% 0.00 [-2.49, 2.49]
François et al., 2020 7.1 2.86 40 6.87 2.78 80 8.5% 0.23 [-0.85, 1.31]
Jiang et al.,2020 10.2 1.8 15 10.57 1.6 15 7.3% -0.37 [-1.59, 0.85]
Knight et al., 2006 1.91 0.57 10 1.53 0.74 10 14.0% 0.38 [-0.20, 0.96]
Koizumi et al., 2016 18.4 5.6 10 14.5 5.2 10 0.8% 3.90 [-0.84, 8.64]
Subtotal (95% CI) 89 129 33.0% 0.27 [-0.19, 0.73]
Heterogeneity: Tau² = 0.00; Chi² = 3.50, df = 4 (P = 0.48); I² = 0%
Test for overall effect: Z = 1.13 (P = 0.26)
1.1.2 Sound dentin (With step rinsing)
Braz et al., 2020 7.5 2.1 7 6.5 4.5 7 1.2% 1.00 [-2.68, 4.68]
Gupta et al., 2019 10.5 10.5 8 22.3 4.4 8 0.3% -11.80 [-19.69, -3.91]
Knight et al., 2006 1.91 0.57 10 2.82 1.38 9 9.5% -0.91 [-1.88, 0.06]
Wang et al., 2016 4 1.68 4 4.25 1.8 4 2.6% -0.25 [-2.66, 2.16]
Subtotal (95% CI) 29 28 13.6% -1.11 [-3.47, 1.25]
Heterogeneity: Tau² = 3.29; Chi² = 8.62, df = 3 (P = 0.03); I² = 65%
Test for overall effect: Z = 0.93 (P = 0.35)
1.1.3 Carious dentin (Without step rinsing)
Braz et al., 2020 12.95 4.41 14 14.4 9.8 14 0.5% -1.45 [-7.08, 4.18]
Jiang et al.,2020 5.97 2.3 15 6.14 2.2 15 5.0% -0.17 [-1.78, 1.44]
Ng et al., 2020 10.4 4.5 10 8.72 5.33 22 1.3% 1.68 [-1.89, 5.25]
Zhao et al., 2019 2.6 1.1 20 2.3 0.9 20 13.4% 0.30 [-0.32, 0.92]
Subtotal (95% CI) 59 71 20.3% 0.26 [-0.31, 0.83]
Heterogeneity: Tau² = 0.00; Chi² = 1.25, df = 3 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.89 (P = 0.37)
1.1.4 Carious dentin (With step rinsing)
Braz et al., 2020 6.5 2.9 7 3.4 2.5 7 2.0% 3.10 [0.26, 5.94]
Puwanawiroj et al., 2019 6.3 4.6 40 7.4 5.1 40 3.2% -1.10 [-3.23, 1.03]
Uchil et a., 2020 1.11 0.56 9 1.61 1.24 27 13.8% -0.50 [-1.09, 0.09]
Wang et al., 2016 4 1.68 4 4.25 1.8 4 2.6% -0.25 [-2.66, 2.16]
Zhao et al., 2019 2.6 1.1 20 3 1.4 20 11.5% -0.40 [-1.18, 0.38]
Subtotal (95% CI) 80 98 33.1% -0.30 [-1.01, 0.41]
Heterogeneity: Tau² = 0.22; Chi² = 6.39, df = 4 (P = 0.17); I² = 37%
Test for overall effect: Z = 0.82 (P = 0.41)
Total (95% CI) 257 326 100.0% -0.09 [-0.51, 0.33]
Heterogeneity: Tau² = 0.24; Chi² = 28.23, df = 17 (P = 0.04); I² = 40%
Test for overall effect: Z = 0.41 (P = 0.68)
Test for subgroup differences: Chi² = 2.98, df = 3 (P = 0.39), I² = 0%
-4
-2
0
2
4
SDF
CONTROL


CONTROL
SDF
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.1.1 Sound dentin (Without step rinsing)
Koizumi et al., 2016 31.83 5.88 30 13.93 7.68 30 8.5% 17.90 [14.44, 21.36]
Kucukyilmaz et al., 2016 36.79 5.37 8 31.87 7.54 8 7.9% 4.92 [-1.49, 11.33]
Lutgen et al., 2018 40.97 4.56 30 11.97 10.42 30 8.4% 29.00 [24.93, 33.07]
Subtotal (95% CI) 68 68 24.8% 17.52 [5.81, 29.22]
Heterogeneity: Tau² = 101.10; Chi² = 41.43, df = 2 (P < 0.00001); I² = 95%
Test for overall effect: Z = 2.93 (P = 0.003)
1.1.2 Sound dentin (With step rinsing)
Firouzmandi et al., 2020 18.37 4.71 6 17.08 4.88 6 8.1% 1.29 [-4.14, 6.72]
Ko et al., 2020 77.5 4.6 16 59.7 6 16 8.5% 17.80 [14.10, 21.50]
Lutgen et al., 2018 40.97 4.56 30 26.8 9 30 8.5% 14.17 [10.56, 17.78]
Markham et al., 2020 28.83 13.47 45 18.5 8.02 45 8.3% 10.33 [5.75, 14.91]
Quock et al., 2012 31.88 5 14 33.57 10.13 14 8.0% -1.69 [-7.61, 4.23]
Selvaraj et al., 2016 28.58 1.1 36 29.28 0.98 36 8.8% -0.70 [-1.18, -0.22]
Wu et al., 2016 162.09 81.08 12 139.85 88.53 12 0.7% 22.24 [-45.68, 90.16]
Subtotal (95% CI) 159 159 50.8% 7.11 [-0.57, 14.79]
Heterogeneity: Tau² = 88.42; Chi² = 176.45, df = 6 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.82 (P = 0.07)
1.1.3 Carious dentin (With step rinsing)
Firouzmandi et al., 2020 12.2 2.34 6 17.63 4.19 6 8.4% -5.43 [-9.27, -1.59]
Siqueira et al., 2020 18.19 3.23 20 25.75 3.01 20 8.7% -7.56 [-9.49, -5.63]
Van Ducker et al., 2019 23.5 10.7 10 19.8 8.4 10 7.4% 3.70 [-4.73, 12.13]
Subtotal (95% CI) 36 36 24.5% -4.79 [-9.19, -0.40]
Heterogeneity: Tau² = 10.00; Chi² = 7.02, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 2.14 (P = 0.03)
Total (95% CI) 263 263 100.0% 7.12 [1.38, 12.85]
Heterogeneity: Tau² = 97.65; Chi² = 542.97, df = 12 (P < 0.00001); I² = 98%
Test for overall effect: Z = 2.43 (P = 0.01)
Test for subgroup differences: Chi² = 16.45, df = 2 (P = 0.0003), I² = 87.8%
-20 -10 0 10 20
SDF CONTROL

4. ARTIGO 3- EVALUATION OF THE USE OF POTASSIUM IODIDE APPLICATION ON STAINED DEMINERALIZED DENTIN UNDER RESIN COMPOSITE FOLLOWING SILVER DIAMINE FLUORIDE APPLICATION

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PEDIATRIC DENTISTRY V 43 / NO 1 JAN / FEB 21

IN VITRO STUDY

Evaluation of the Use of Potassium Iodide Application on Stained Demineralized Dentin Under Resin Composite Following Silver Diamine Fluoride Application

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Abstract: ***Purpose:*** *The purpose of this study was to assess the effect of potassium iodide (KI) after applying silver diamine fluoride (SDF) on the staining of demineralized dentin covered or not by a composite resin layer.* ***Methods:*** *Dentin blocks from 30 bovine incisors were demineralized and randomly allocated in three groups (n equals 10): (1) control (no treatment); (2) treated with SDF; and (3) treated with SDF and KI. Half of the specimens of each group received a composite resin restoration immediately after treatment. A colorimetric evaluation, accordingto the CIE L*a*b* system, was performed at baseline and after seven, 14, 30, and 60 days. The ΔE data were analyzed using the generalized linear model (Δ equals 0.05).* ***Results:*** *The use of KI immediately after applying SDF decreased the dentin staining at all assessment times. SDF treatment only stained the dentin under composite resin after 60 days. The application of KI reduced the dentin under composite resin staining as ΔE values were similar to the control group even after 60 days.* ***Conclusions:*** *The use of potassium iodide minimizes the darkening of dentin and prevents the staining of the dentin under composite resin restorations in the long-term. (Pediatr Dent 2021;43(1):) Received / Last Revision / Accepted*

KEYWORDS: SILVER DIAMINE FLUORIDE, POTASSIUM IODIDE, DENTIN, COMPOSITE RESIN, DISCOLORATION

The use of silver diamine fluoride (**SDF**) was first proposed from Japan in the late 1960s[1,2] Although not prominently used subsequent to its first reports, it resurfaced in the early 2000s and returned to prominence mainly after its introduction in the American market in 2014,[3] approved by the U.S. Food and Drug Administration to decrease hypersensitivity. Its off-label use for primary teeth caries arrest is effective according to several recent systematic reviews that demonstrate its effectiveness in arresting caries in primary teeth.[4-7]

Besides its traditional use in arresting carious lesions, SDF can also be applied before composite resin restorations.[8,9] In vitro studies demonstrate that SDF application before restoration can prevent secondary caries in glass ionomer and composite resin restorations.[10,11] Moreover, as long as the protocol includes the water-washing step after SDF, this application does not jeopardize the bond strength of the restorative material.[12]

Despite the benefits attributed to SDF, an inherent disadvantage of its use is that it darkens the treated areas[13] by oxidizing silver ions,[14] and this clinical observation can be a significant impediment to its use. In an attempt to minimize this effect, the use of a potassium iodide solution (**KI**) after its application has been suggested.[15,16] Previous studies confirm that the staining potential of SDF is modified when the KI solution is used.[17-20] However, in some of these studies[18,20] it was applied to sound dentin, and it is known that a higher concentration of precipitate is formed in demineralized dentin[21] and greater staining is also observed in this altered substrate.[22] Also, the effect of the KI application was only evaluated for up to four weeks[19,20] after treatment, so studies with a longer time of observation are still needed.

Few studies have evaluated the staining effect of SDF, combined or not with KI, applied immediately before restorative treatment. KI application reduces the marginal staining of glass ionomer cement restoration,[19,23] resin-modified glass ionomer, and glass ionomer combined with composite resin restorations.[19] Also, a recently published systematic review pointed out that the available evidence is not sufficient to show the advantage of KI associated with SDF in reducing tooth staining.[24]

No previous study evaluated the staining of composite resin placed directly on the SDF-treated dentin. In a previous study,[19] SDF-treated dentin was first covered by a layer of a resin-modified glass ionomer before the composite resin placement, preventing the perception of the SDF staining on the composite resin.

The purpose of this study was to assess the effect of combined use of silver diamine fluoride and potassium iodide in the staining of demineralized dentin covered or not by composite resin. The null hypothesis tested was that there is no difference between the treatment with SDF and SDF combined with KI in the staining of the demineralized dentin covered or not by a composite resin layer.

Methods

Sample preparation. Thirty bovine incisors free of cracks and opacities were selected for this study from a collection obtained in a slaughterhouse, without the need for prior approval by

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an institutional review board. The sample size was based on several previous studies that assessed color stability.[17,25,26] The roots of the teeth were sectioned below the cementoenamel junction, with a diamond disk in a cutting machine (Labcut 1010, Extec Corp., Enfield, Conn., USA), and each tooth was sectioned in the middle-third, generating a two-mm-thick dentin block between the buccal surface and pulp chamber. A digital caliper was used to measure the dimensions of the blocks. The buccal surface of each block was abraded using 600-grit silicon carbide papers under running water to create a flat dentin surface.

Artificial caries induction by pH cycling. The specimens (dentin blocks) were submitted to the cariogenic challenge by pH cycling to create artificial demineralized dentin. Two layers of colorless cosmetic nail enamel (fingernail polish) were applied for insulation of the surfaces of the specimens, except the buccal surface. They were immersed individually in 10 ml of demineralizing solution (2.2 mM $CaCl_2$, 2.2 mM NaH_2PO_4, 0.05 M acetic acid adjusted to pH 4.8 with one M KOH) for eight hours and in 10 ml of remineralizing solution (1.5 mM $CaCl_2$, 0.9 mM NaH_2PO_4 and 0.15 mM KCl adjusted to pH 7.0), for eight hours, totaling 14 days.[27,28]

Dentin treatment. The specimens were randomly allocated into three groups according to the dentin treatment (N equals 10 per group). All treatments were performed by a single trained operator. In the control group, the dentin blocks were not treated. In the SDF group, specimens received one application of 38 percent SDF solution (Step 1, Riva Star, SDI, Bayswater, Australia), which was applied with a disposable microbrush for 60 seconds following the manufacturer's instructions. In the specimens from the SDF+KI group, SDF was applied (as SDF group) and followed immediately with application of KI (Step 2, Riva Star, SDI) until the formed creamy white color turned clear, leaving the products to dry on the dentin surface, as recommended by the manufacturer.

Five specimens of each group were used to evaluate the dentin staining, and the remaining specimens were immediately restored with composite resin. Before restorations and after application of KI, in the SDF+KI group specimens the dentin surface was washed with water for at least 10 seconds and air-dried, as recommended by the manufacturer.

Bonding and restorative procedures. After acid etching, the adhesive system (Adper Single Bond Plus, 3M ESPE, St. Paul, Minn., USA) was applied to demineralized and treated dentin according to the manufacturer's instructions. A metal matrix with dimensions of six by six by one mm, used to standardize the restorations, was placed on the specimen and filled with composite resin (Filtek Z 350 A2d, 3M ESPE) and light-cured for 20 seconds. The thickness of the specimen (dentin blocks plus composite resin) was confirmed with a digital caliper and should measure approximately three mm in thickness.

Colorimetric assessment. The specimens' were stored in deionized water at 37 degrees Celsius until the colorimetric assessment, which was performed at baseline immediately after treatment for dentin specimens and immediately after restorative procedures for dentin under composite resin restoration specimens) after seven, 14, 30, and 60 days. The methods used were similar to those commonly employed in color science. The color assessment was done using a spectrophotometer (SP60, X-Rite, Grandville, Mich., USA) in analyzing mode using a D65 illuminant (which represents the average color temperature of daylight). The specimens were placed in the center of the spectrophotometer with a coupling medium (glycerin) to simulate the oral environment color evaluation conditions,[25] and the color assessment was performed three times for each specimen by a single trained operator who was blinded for the treatment groups. Before each assessment, the instrument was calibrated according to the manufacturer's recommendation.

The Commission Internationale d'Eclairage (**CIE**) L*a*b system values were obtained and used to calculate the color changes (**ΔE**) for each assessment time by applying the following CIEDE2000 color difference equation[29]:

$$\Delta E' = [(\Delta L'/K_L S_L)^2 + (\Delta C'/K_C S_C)^2 + (\Delta H'/K_H S_H)^2 + R_T(\Delta C'/K_C S_C)(\Delta H'/K_H S_H)]^{1/2}$$

For composite resin samples, clinical acceptance was assessed using reference values from a previous study.[30] An ΔE higher than 1.8 cannot be considered as clinically acceptable.

Statistical analyses. The normal distribution of the data was not confirmed by the Kolmogorov-Smirnov test. The means ΔE values were analyzed by the general linear model separately for dentin specimens and resin composite restorations. For each analysis, dentin treatment and assessment time were considered the main factors. Statistical analysis was performed considering a significance level of five percent using Minitab Express software, version 1.5.3 (Minitab Inc., State College, Pa., USA).

Table 1. COLOR CHANGES (ΔE VALUES) FOR DENTIN SPECIMENS (WITHOUT RESIN COMPOSITE RESTORATION)*

Group	Assessment time			
	7 days Mean±(SD)	14 days Mean±(SD)	30 days Mean±(SD)	60 days Mean±(SD)
Control	2.46 (1.99)	3.53 (1.74)	4.70 (1.95)	5.52 (2.66)
SDF	26.30 (4.65)	29.75 (5.49)	32.71 (5.32)	32.44 (6.16)
SDF+KI	8.48 (2.77)	9.80 (4.81)	16.98 (8.44)	19.96 (5.14)

* According to the silver diamine fluoride treatment (group) and assessment time. Each group (treatment x assessment time): N=5; SD=standard deviation.

Table 2. COMPARISON AMONG COLOR CHANGES (ΔE VALUES)* FOR DENTIN SPECIMENS (WITHOUT RESIN COMPOSITE RESTORATION)

SDF treatment†	ΔE§
Control	4.06 (2.27)^{A}
SDF	30.3 (5.65)^{B}
SDF+KI	13.81 (7.16)^{C}
Assessment time‡	**ΔE§**
7 days	12.41 (10.92)^{A}
14 days	14.36 (12.25)^{A,B}
30 days	18.13 (13.05)^{B,C}
60 days	19.31 (12.52)^{C}

* Presented as means±(standard deviation).

† According to the SDF treatment (group), each SDF treatment group: N=20.

‡ According to assessment time, each assessment time group: N=15.

§ Different superscript letters indicate statistically significant differences (general linear model; P=0.001) in rows comparisons for silver diamine fluoride treatment and assessment time, separately.

r^2

Table 3. COMPARISON AMONG COLOR CHANGES (ΔE VALUES)*† FOR COMPOSITE RESIN RESTORATIONS‡

Group	Assessment time			
	7 days	14 days	30 days	60 days
Control	1.18 (0.23)^{B,C}	1.51 (0.64)^{B,C}	1,29 (0.57)^{B,C}	1.41 (0.56)^{B,C}
SDF	2.63 (1.57)^{A,B,C}	2.50 (0.9)^{B,C}	3.32 (1.8)^{A,B}	4.79 (1.61)^{A}
SDF+KI	1.11 (0.34)^{C}	1.75 (0.64)^{B,C}	2.00 (0.73)^{B,C}	2.31 (1.00)^{B,C}

* Presented as means±(standard deviation); SDF=silver diamine fluoride; KI=potassium iodide.

† Different superscript letters indicate statistically significant differences (general linear model; P=0.000) among groups.

‡ According to the silver diamine fluoride treatment (group) and assessment time; each group (treatment x assessment time): N=5.

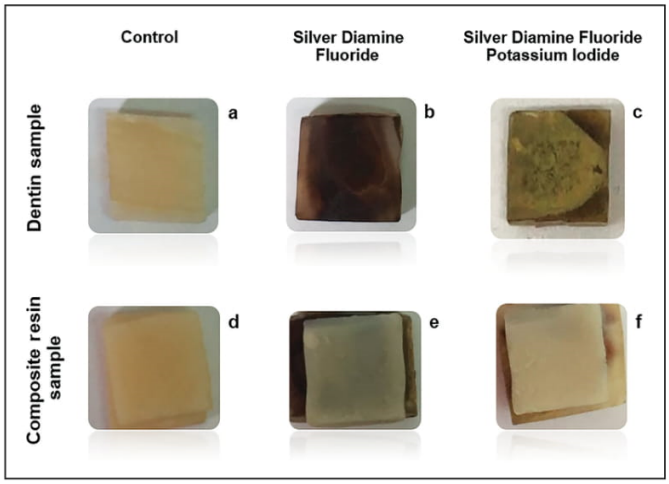

Figure. Illustrative images of the dentin and composite resin specimens at the final assessment time (day 60): (a) dentin specimen without silver diamine fluoride (SDF) treatment; (b) dentin specimen with SDF application; (c) dentin specimen with potassium iodide (KI) application following SDF application; (d) dentin without SDF treatment under composite resin specimen; (e) dentin with SDF application under composite resin specimen; (f) dentin with KI application following SDF application under composite resin specimen.

Results

Dentin color alteration. Table 1 shows the ΔE values for dentin according to the experimental groups. All groups presented color changes after water storage, including the control group (untreated dentin block). Only the main factors dentin treatment and assessment time were statistically significant (both P<0.001). The cross-interaction (dentin treatment versus assessment time) was not statistically significant (P=0.33). Thus, the ΔE values are presented in Table 2, considering the comparison among the three treatment groups separately (disregarding the assessment time; N equals 20) and the assessment time (disregarding treatment; N equals 15). Therefore, the treatment effect on dentin color changes was not dependent on the assessment time, and dentin color changes over assessment time occurred in the same way regardless of treatment. Both SDF treatments (SDF and SDF+KI groups) caused significant dentin staining, as their ΔE values were higher compared to the control group (untreated dentin block; P<0.001). The use of KI after SDF (SDF+KI group) significantly reduced the dentin staining, though not entirely. Dentin color changes seem to increase over time, as ΔE values obtained after 30 and 60 days were statistically higher than the seven days values.

Resin composite color alteration. The ΔE values for experimental groups are shown in Table 3. Statistically significant differences were found for the interaction between dentin treatment and assessment time (P=0.000). No statistically significant differences among the ΔE values obtained for the control, SDF, and SDF+KI groups were found after considering the assessment time of seven, 14, and 30 days of water storage. After 60 days, the values of the SDF group were higher than those obtained for the control (untreated dentin) and SDF+KI groups. The color measurements of the control and SDF+KI groups were stable over time; however, the SDF+KI group presented an upward trend in values, although it was not statistically significant.

Exemplary photos of dentin and resin composite samples from each SDF treatment group at the last assessment time can be seen in the Figure.

Discussion

Black staining of arrested carious lesions is the main adverse effect associated with the use of SDF.[13] In an attempt to minimize this effect, the subsequent application of a KI solution has been suggested.[15,16] It is speculated that KI prevents staining through the precipitation of excess silver ions as white silver iodide.[19] However, a recent systematic review points out that still there is insufficient evidence to support its benefit in reducing tooth staining, besides that the included primary studies had differing study designs and were limited to 30 days follow-up.[24] This in vitro study considered a longer evaluation time after SDF application, the demineralized dentin color change, and the color alteration after covered by resin composite. Thus, the tested null hypothesis, that there is no difference between the use of KI or not in the staining of demineralized dentin covered or not by a composite resin layer, was rejected.

In the present study, SDF treatment was responsible for darkening the demineralized dentin. However, the subsequent application of KI minimizes this negative effect. This can be explained by the reaction of the iodine ions with the excess of silver ions that form a precipitate of silver iodide, a creamy white reaction product.[16] This finding agrees with previous studies,[17-20] but some of these studies had applied the product in sound dentin,[18,20] and it is known that less staining is observed on this substrate.[22] Besides, a longer follow-up period was considered in the present study and it was possible to observe that, even after 30 days, there was still an intensification of dentin darkening in SDF treatments. The water storage period and the demineralized dentin condition could explain the color changes and values variability observed for specimens not covered by composite resin. Besides the continuous chemical dissolution of the mineral phase in water,[31] the dehydration of the specimens before color measurements may also be associated, as rehydration does not always occur completely,[32,33] being an inherent condition and a limitation of laboratory studies.

A previous study[19] also evaluated the color change of composite resin placed after dentin treated with SDF; however, a layer of light-cured resin-modified glass ionomer was applied over the dentin before the composite resin placement, which

can prevent the perception of SDF staining. In the present study, the composite resin restoration was placed directly on the treated dentin. The present study's results suggest that significant staining of the dentin under composite resin by SDF occurred only after 60 days of storage. It is important to consider that visual color thresholds can serve as a quality control tool to evaluate restorative materials; thus, SDF causes unacceptable color changes already after seven days. The application of KI solution significantly reduced the color change of dentin under composite resin; unacceptable color change values were found at 30 days.

In the present study, the composite resin Z350 XT dentin shade was chosen because it is less translucent, with a good masking performance.[26] For spectrophotometer evaluation, the thickness of the composite resin restoration had to be only one mm, probably reducing its masking capacity. However, the purpose of this study was not to assess the masking capacity or the staining of the composite resin but instead assess the staining of the dentin resulting from SDF treatment and whether the resin composite placed immediately after dentin treatment would be able to prevent or minimize the staining. Nevertheless, it is important to note that, in this study, it was not possible to assess the influence on marginal staining; this should be investigated in future research.

In this study, the color change was assessed with a digital spectrophotometer, the most used method in previous studies.[18,20,23] Unlike published studies, which assessed the influence of SDF and SDF+KI on dentin and restorative material color change, in the present study a neutral gray background was used[25,34] to avoid the influence of the black and white background, commonly used in color studies, as dentinal specimens were thin. Moreover, the CIEDE2000 instead of the CIELAB formula used to calculate the color alteration in this study seems to be more accurate and sophisticated,[35] and it uses the hue and chrome concepts.[36] Bovine teeth have been used in laboratory research as an alternative to human teeth mainly due to the ease in obtaining a collection of bovine teeth and the possibility of standardizing the tooth age, diet, and other environmental conditions, thus reducing the variability among specimens.[18] Bovine teeth behave similarly to human teeth in terms of staining and bleaching effect[37] because of the similar chemical composition, density, and microhardness.[38,39] Furthermore, the use of bovine teeth does not require the consent and approval by an ethics committee, since they come from animals already slaughtered for other purposes.[40]

Within the limitations of an in vitro study, this research shows that the application of KI after the SDF can minimize dentin darkening and also prevent the staining of composite resin restorations in the long term. It is important to note that there are still doubts regarding the effectiveness of SDF and SDF with KI for caries prevention. A previous study[23] suggested that SDF combined with KI is not as effective as SDF alone at secondary caries prevention, and another study reported that SDF used with KI was more effective than SDF alone at inhibiting *Streptococcus mutans* migration through dentin.[41] Hence, more studies evaluating the effectiveness of SDF+KI are required. If aesthetics are of concern, the combined use of SDF with KI can promote dentin color stability and be preferred over SDF alone. Still, further laboratory and clinical studies are needed to confirm these findings.

Conclusions

Based on this study's results, the following conclusions can be made:

1. Silver diamine fluoride can stain demineralized dentin, even with the subsequent application of potassium iodide.
2. The use of KI significantly reduces dentin darkening.
3. The use of KI is useful in preventing the dentin's staining under composite resin restorations.

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5. DISCUSSÃO

O diamino fluoreto de prata é utilizado no Brasil há décadas; porém, recentemente, tem despertado maior interesse e talvez uma maior utilização, por ser uma técnica não invasiva para o tratamento de lesões cárie. Contudo, a observação clínica de que ele causa o escurecimento da estrutura dentária tratada (LLODRA et al., 2005) pode ser um impedimento significativo para seu uso, e também na sua inclusão no ensino em cursos de graduação em Odontologia. Diante disso, surgiu a questão de pesquisa que gerou o primeiro artigo que compõe esta tese, intitulado "Teaching and use of silver diamine fluoride in Pediatric Dentistry: Questionnaire-based cross-sectional analysis of undergraduate Brazilian dental schools". Este é o primeiro estudo a investigar o uso do diamino fluoreto de prata nos cursos de graduação em Odontologia do Brasil.

Os resultados obtidos no estudo mostram que o DFP é tópico de aulas teóricas e é utilizado na prática clínica da maioria dos cursos de Odontologia brasileiros. Todas as instituições que atestam a utilização do DFP, o utilizam em dentes decíduos, principalmente em lesões cavitadas em dentina, de crianças ente 0 e 3 anos. Este resultado corrobora com o encontrado na literatura, uma vez que o DFP tem sido considerado o tratamento não invasivo mais eficaz para paralisação de lesões de cárie em dentes decíduos (CHIBINSKI et al., 2017), principalmente em lesões cavitadas (SLAYTON et al., 2018; CORRÊA-FARIA et al., 2020), especialmente envolvendo dentina (TEDESCO et al., 2018), tendo como principal indicação o tratamento de cárie na primeira infância, onde o comportamento não cooperativo, pode ser considerado uma barreira ao tratamento restaurador tradicional (AMERICAN ACADEMY OF PEDIATRIC DENTISTRY 2017). Além disso, em uma parcela considerável das instituições o seu uso está restrito aos dentes posteriores, provavelmente devido ao potencial de escurecimento da área afetada em que o DFP é aplicado (LLODRA et al., 2005), sendo menos aceitável em dentes anteriores (CRYSTAL et al.,2017). Também, o DFP não é comumente utilizado em dentes permanentes na maioria das instituições brasileiras, provavelmente devido à maior demanda estética para estes dentes.

Quase metade das escolas entrevistadas relatou utilizar o DFP há menos de cinco anos e o recente interesse da comunidade científica pode ter contribuído para isso. É importante considerar também que, embora a maioria das instituições brasileiras relatem o uso, ele é pouco frequente. Foi possível observar que há escolas que o usam raramente ou até mesmo nunca o usam. Portanto, o presente estudo é relevante por trazer um panorama atual do ensino do diamino fluoreto de prata e incentivar a sua inclusão nos cursos de graduação em Odontologia,

tanto no ensino teórico como na rotina clínica, visto que é uma tratamento bem estabelecido e bem-sucedido para lesões de cárie, principalmente em dentes decíduos.

Recentemente, a aplicação do diamino fluoreto de prata previamente a uma restauração tem sido sugerida pela literatura, para prevenção de lesões de cárie secundárias (WU et al., 2016; WANG et al.,2016; KUCUKYLMAZ et al., 2016). Diante disso, os outros dois artigos que compões esta tese são estudos que foram desenvolvidos para avaliar o efeito do DFP sobre os tecidos dentários e restaurações subsequentes ao seu uso.

O segundo artigo apresentado nesta tese, "Bonding of glass-ionomer cement and adhesive systems to silver diamine fluoride-treated dentine: An updated systematic review and meta-analysis", foi desenvolvido diante a necessidade de uma atualização de uma revisão sistemática (FRÖHLICH et al., 2020), que avaliou a influência da aplicação prévia de DFP na adesão de materiais restauradores diretos à dentina. Nesta primeira revisão, a grande maioria dos estudos incluídos avaliou a aplicação de DFP em dentina hígida, portanto, uma análise independente com dados de dentina afetada por cárie, um relevante substrato, não pode ser investigada. Após a sua publicação, novos estudos avaliando a aplicação de DFP em dentina afetada por cárie foram publicados, sem, no entanto,existir consenso de resultados.

Os resultados da presente revisão sistemática mostram que a aplicação prévia de DFP não influencia a resistência de união do cimento de ionômero de vidro à dentina hígida ou afetada por cárie. Por outro lado, pode prejudicar a adesão dos sistemas adesivos. No entanto, a etapa de enxágue após o DFP elimina esse efeito adverso na dentina hígida e parece melhorar a resistência de união dos sistemas adesivos à dentina afetada por cárie, um relevante achado. A etapa de lavagem imediatamente após a aplicação do DFP pode eliminar o excesso de precipitado de prata da dentina peritubular e intertubular (LUTGEN et al., 2018), favorecendo a adesão. Além disso, o DFP pode remineralizar a dentina afetada por cárie (ZHAO et al., 2018), melhorando a adesão à este substrato alterado. Contudo, esse último achado foi obtido com base em apenas 3 estudos, portanto são incentivadas mais investigações avaliando o mecanismo de adesão dos sistemas adesivos à dentina afetada por cárie tratada com DFP para confirmar este resultado.

É importante considerar que, a proposta de aplicação de DFP previamente a um material restaurador é nova, no entanto, é possível observar que, logo após a publicação da primeira revisão sistemática, o dobro de artigos pode ser incluído nesta atualização, demonstrando o crescente interesse nesta proposta de utilização. Apesar do aumento considerável no número de estudos, apenas um novo estudo avaliando dentes decíduos foi incluído e uma meta-análise separada ainda não pode ser realizada. Além disso, apenas um estudo avaliou o efeito da

aplicação de DFP na resistência de união após armazenamento, com isso, a influência do envelhecimento também não pode ser avaliada por meio de uma meta-análise.

A relevância dos resultados deste estudo reside em propor um melhor protocolo de aplicação do DFP quando uma restauração for realizada imediatamente após seu uso. Diante da evidência gerada por essa revisão sistemática com meta-análise de estudos laboratoriais, a aplicação prévia de diamino fluoreto de prata não afeta a adesão dos cimentos de ionômero de vidro, contudo, se o material restaurador for a resina composta, a lavagem após a aplicação do DFP parece ser um passo essencial.

O terceiro artigo desta tese, intitulado “Evaluation of the use of potassium iodide application on stained demineralized dentin under resin composite following silver diamine fluoride application” (FRÖHLICH et al., 2021), objetivou avaliar o efeito do uso de diamino fluoreto de prata combinado ou não com o iodeto de potássio na coloração da dentina desmineralizada coberta ou não por resina composta. Os resultados apresentados neste estudo demonstram que os tratamentos com DFP são responsáveis pelo escurecimento da dentina desmineralizada. No entanto, a aplicação subsequente de iodeto de potássio foi capaz de minimizar esse efeito negativo. Isso pode ser explicado pela reação dos íons de iodo com o excesso de íons de prata que formam um precipitado de iodeto de prata, um produto de reação branco cremoso (PATEL et al., 2018). Esse achado concorda com estudos anteriores (PATEL et al., 2018; SAYED et al., 2018; NGUYEN et al., 2017; ESPÍNDOLA-CASTRO et al., 2020), porém alguns desses estudos haviam realizado a aplicação do produto em dentina hígida, e sabe-se que um menor manchamento é observado neste substrato (KNIGHT et al., 2007). Além disso, um período de acompanhamento mais longo foi considerado no presente estudo, sendo possível observar que, mesmo após 30 dias, houve ainda uma intensificação do escurecimento da dentina nos tratamentos com DFP. A aplicação da solução de iodeto de potássio reduziu significativamente a mudança de cor da dentina sob resina composta à longo prazo. A aplicação de DFP causou mudanças de cor da dentina sob resina composta inaceitáveis logo após sete dias, já no grupo da associação com iodeto de potássio valores de mudança de cor inaceitáveis foram encontrados somente após 30 dias. É válido ressaltar, contudo, que neste estudo não foi avaliada a influencia no manchamento marginal das restaurações de resina composta, fato que deve ser investigado em futuras pesquisas. Com base no exposto, este estudo sugere que, se a estética for motivo de preocupação, o uso combinado de diamino fluoreto de prata com iodeto de potássio é preferível, uma vez que pode minimizar o manchamento da dentina e promover a estabilidade da cor da dentina sob uma restauração de resina composta.

Portanto, nesta tese, são apresentadas evidências sobre o ensino do DFP no Brasil, e incentiva a sua maior utilização, tanto nas disciplinas de Odontopediatria dos cursos de graduação, como também na rotina clínica da especialidade. Também, através do estudo laboratorial e da revisão sistemática apresentados, protocolos de uso são sugeridos para restaurações realizadas imediatamente após a aplicação do diamino fluoreto de prata, especialmente quando a resina composta for o material utilizado. Contudo, a indicação da inclusão do diamino fluoreto de prata no protocolo restaurador é recente e estudos laboratoriais e clínicos são ainda necessários para permitir seu uso como rotina.

6. CONCLUSÃO

Com base nos resultados obtidos pelos três artigos que compõe essa tese, conclui-se que:

- O diamino fluoreto de prata tem sido considerado tópico de ensino teórico nas disciplinas de Odontopediatria na maioria das escolas de odontologia Brasileiras. Contudo, seu uso ainda é pouco frequente. Além disso, pode-se observar que é utilizado principalmente para tratamento da cárie na primeira infância, em lesões cavitadas nos dentes decíduos posteriores.

- A aplicação prévia de diamino fluoreto de prata não prejudica a adesão do cimento de ionômero de vidro à dentina hígida e afetada por cárie. O mesmo é válido para os sistemas adesivos, desde que a etapa de enxágue após a sua aplicação seja realizada. Essa etapa se mostrou capaz de aumentar a adesão dos sistemas adesivos à dentina afetada por cárie.

- O diamino fluoreto de prata ocasiona o manchamento da dentina desmineralizada, mesmo com a aplicação subsequente de iodeto de potássio. Contudo, o uso de iodeto de potássio pode minimizar esse escurecimento da dentina. Esse passo adicional após a aplicação do DFP também se mostrou capaz de evitar, em longo prazo, o manchamento da dentina sob restaurações de resina composta realizadas imediatamente após o tratamento.

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ANEXO A- NORMAS PARA PUBLICAÇÃO NO PERIÓDICO *REVISTA DA ABENO*

Normas para Apresentação

Missão -A Revista da ABENO -Associação Brasileira de Ensino Odontológico é uma publicação quadrimestral que tem como missão primordial contribuir para a obtenção de indicadores de qualidade do ensino Odontológico, respeitando os desejos de formação discente e capacitação docente, com vistas a assegurar o contínuo progresso da formação profissional e produzir benefícios diretamente voltados para a coletividade. Visa também produzir junto aos especialistas a reflexão e análise crítica dos assuntos da área em nível local, regional, nacional e internacional. ¬Originais - Os originais deverão ser redigidos em português ou inglês e digitados na fonte Arial tamanho 12, em página tamanho A4, com espaço 1,5 e margem de 3 cm de cada um dos lados, perfazendo o total de no máximo 17 páginas, incluindo quadros, tabelas e ilustrações (gráficos, desenhos, esquemas, fotografias etc.) ou no máximo 25.000 caracteres contando os espaços.¬Ilustrações - As ilustrações (gráficos, desenhos, esquemas, fotografias etc.) deverão ser limitadas ao mínimo indispensável, apresentadas em páginas separadas e numeradas consecutivamente em algarismos arábicos. As respectivas legendas deverão ser concisas e localizadas abaixo e precedidas da numeração correspondente. Nas tabelas e nos quadros a legenda deverá ser colocada na parte superior. As fotografias deverão ser fornecidas em mídia digital, em formato tif ou jpg, tamanho 10 x 15 cm, em no mínimo 300 dpi. Não serão aceitas fotografias em Word ou Power Point. Deverão ser indicados os locais no texto para inserção das ilustrações e de suas citações.¬Encaminhamento de originais – Solicita-se o encaminhamento dos originais de acordo com as especificações descritas emhttp://revabeno.emnuvens.com.br/revabeno/. A submissão on-line é simples e segura¬A estrutura do original

1.Cabeçalho: Quando os artigos forem em português, colocar título e subtítulo em português e inglês; quando os artigos forem em inglês, colocar título e subtítulo em inglês e português. O título deve ser breve e indicativo da exata finalidade do trabalho e o subtítulo deve contemplar um aspecto importante do trabalho.2.Autores: Indicação de apenas um título universitário e/ou uma vinculação à instituição de ensino ou pesquisa que indique a sua autoridade em relação ao assunto. 3.Resumo: Representa a condensação do conteúdo, expondo metodologia, resultados e conclusões, não excedendo 250 palavras e em um único parágrafo.4.Descritores: Palavras ou expressões que identifiquem o conteúdo do artigo. Para suadeterminação, consultar a lista de "Descritores em Ciências da Saúde -DeCS" (http://decs.bvs.br) (no máximo 5). 5.Texto: Deverá seguir, dentro do possível, a seguinte estrutura:

a)Introdução: deve apresentar com clareza o objetivo do trabalho e sua relação com os outros trabalhos na mesma linha ou área. Extensas revisões de literatura devem ser evitadas e quando possível substituídas por referências aos trabalhos mais recentes, onde certos aspectos e revisões já tenham sido apresentados. Lembre-se que trabalhos e resumos de teses devem sofrer modificações de forma a se apresentarem adequadamente para a publicação na Revista, seguindo-se rigorosamente as normas aqui publicadas.b)Material e métodos: a descrição dos métodos usados deve ser suficientemente clara para possibilitar a perfeita compreensão e repetição do trabalho, não sendo extensa. Técnicas já publicadas, a menos que tenham sido modificadas, devem ser apenas citadas (obrigatoriamente).c)Resultados: deverão ser apresentados com o mínimo possível de discussão ou interpretação pessoal, acompanhados de tabelas e/ou material ilustrativo adequado, quando necessário. Dados estatísticos devem ser submetidos a análises apropriadas.d)Discussão: deve ser restrita ao significado dos dados obtidos, resultados alcançados, relação do conhecimento já existente, sendo evitadas hipóteses

não fundamentadas nos resultados. e)Conclusões: devem estar baseadas no próprio texto. f)Agradecimentos (quando houver).6.Abstract: Resumo do texto em inglês. Sua redação deve ser paralela à do resumo em português.7.Descriptors: Versão dos descritores para o inglês. Para sua determinação, consultar a lista de “Descritores em Ciências da Saúde - DeCS” (http://decs.bvs.br) (no máximo 5).8.Referências: Devem ser normatizadas de acordo com o Estilo Vancouver, conforme orientações publicadas no site da “National Library of Medicine” (http://www.nlm.nih.gov/bsd/uniform_req uirements.html). Para as citações no corpo do texto deve-se utilizar o sistema numérico, no qual são indicados no texto somente os números-índices na forma sobrescrita. A citação de nomes de autores só é permitida quando estritamente necessária e deve ser acompanhada de número-índice e ano de publicação entre parênteses. Todas as citações devem ser acompanhadas de sua referência completa e todas as referências devem estar citadas no corpo do texto. As abreviaturas dos títulos dos periódicos deverão estar de acordo com o List of Journals Indexed in Index Medicus (http://www.ncbi.nlm.nih.gov/entrez/query .fcgi?db=journals). A lista de referências deve seguir a ordem em que as mesmas são citadas no texto. A exatidão das referências é de responsabilidade dos autores.9.Autor correspondente, com e-mail e endereço.

ANEXO B- NORMAS PARA PUBLICAÇÃO NO PERIÓDICO *THE JOURNAL OF ADHESIVE DENTISTRY*

The Journal of Adhesive Dentistry is a bi-monthly journal that publishes scientifically sound articles of interest to practitioners and researchers in the field of adhesion to hard and soft dental tissues. The Journal publishes several types of peer-reviewed original articles:

1. **Clinical and basic science research reports** – based on original research in adhesive dentistry and related topics.
2. **Reviews topics** – on topics related to adhesive dentistry
3. **Short communications** – of original research in adhesive dentistry and related topics. Max. 4 printed pages, including figures and references (max. characters 18,000). High priority will be given to the review of these papers to speed publication.
4a. I**nvited focus articles** – presenting a position or hypothesis on a basic science or clinical subject of relevant related topics. These articles are not intended for the presentation of original results, and the authors of the articles are selected by the Editorial Board.
4b. **Invited commentaries** – critiquing a focus article by addressing the strong and weak points of the focus article. These are selected by the Editorial Board in consultation with the focus article author, and the focus article and the commentaries on it are published in sequence in the same issue of the Journal.
5. **Invited guest editorials** – may periodically be solicited by the Editorial Board.
6. **Proceedings of symposia, workshops, or conferences** – covering topics of relevance to adhesive dentistry and related topics.
7. **Letters to the Editor** – may be submitted to the editorin-chief; these should normally be no more than 500 words in length.

SUBMISSION INSTRUCTIONS
Submission of manuscripts in order of preference:

1.Submission via online submission service (www.manuscriptmanager.com/jadd). Manuscript texts should be uploaded as PC-word files with tables and figures preferably embedded within the PC-word document. A broad range of file formats are acceptable. No paper version required but high resolution photographs or illustrations should be sent to the editorial office (see below). Online submissions are automatically uploaded into the editorial office's reviewer assignment schedule and are therefore processed immediately upon upload.
2.Submission via e-mail as a PC-word document (wintonowycz@quintessenz.de). Illustrations can be attached in any format that
can be opened using Adobe Photoshop, (TIF, GIF, JPG, PSD, EPS etc.) or as Microsoft PowerPoint Documents (ppt). No paper version required but high resolution photographs or illustrations should be sent to the editorial office.
3. One paper copy of the manuscript plus a floppy diskette or CD-ROM (mandatory) containing a PC-word file of the manuscript text, tables and legends. Figures should be included on the disk if possible in any format that can to be opened using Adobe Photoshop, (TIf, GIf, JPG, PSD, EPS etc.) or as a Microsoft PowerPoint Document (ppt)

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Illustrations that cannot be sent electronically will be scanned at the editorial office so that they can be sent to reviewers via e-mail along with the manuscript to expedite the evaluation process. Resubmitted manuscripts should also be submitted in the above manner. Please note that supplying electronic versions of your tables and illustrations upon resubmission will assure a faster publication time if the manuscript is accepted.

Review/editing of manuscripts. Manuscripts will be reviewed by the editor-in-chief and at least two reviewers with expertise within the scope of the article. The publisher reserves the right to edit accepted manuscripts to fit the space available and to ensure conciseness, clarity, and stylistic consistency, subject to the author's final approval. **Adherence to guidelines.** Manuscripts that are not prep ared in accordance with these guidelines will be returned to the author before review.

MANUSCRIPT PREPARATION

• The Journal will follow as much as possible the recommendations of the International Committee of Medical Journal Editors (Vancouver Group) in regard to preparation of manuscripts and authorship (Uniform requirements for manuscripts submitted to biomedical journals. Ann Intern Med 1997;126: 36-47).

• **Title page.** The first page should include the title of the article (descriptive but as concise as possible) and the name, degrees, job title, professional affiliation, contribution to the paper (e.g., idea, hypothesis, experimental design, performed the experiments in partial fulfillment of requirements for a degree, wrote the manuscript, proofread the manuscript, performed a certain test, consulted on and performed statistical evaluation, contributed substantially to discussion, etc.) and full address of all authors. Phone, fax, and e-mail address must also be provided for the corresponding author, who will be assumed to be the first listed author unless otherwise noted. If the paper was presented before an organized group, the name of the organization, location, and date should be included.

• **3-8 keywords**.

• **Structured abstract**. Include a maximum 250-word structured abstract (with headings Purpose, Materials and Methods, Results, Conclusion).

• **Introduction.** Summarize the rationale and purpose of the study, giving only pertinent references. Clearly state the working hypothesis.

• **Materials and Methods.** Present materials and methods in sufficient detail to allow confirmation of the observations. Published methods should be referenced and discussed only briefly, unless modifications have been made. Indicate the statistical methods used, if applicable.

• **Results.** Present results in a logical sequence in the text, tables, and illustrations. Do not repeat in the text all the data in the tables or illustrations; emphasize only important observations.

• **Discussion.** Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the Introduction or Results section. Relate observations to other relevant studies and point out the implications of the findings and their limitations.

• **Acknowledgments**. Acknowledge persons who have made substantive contributions to the study. Specify grant or other financial support, citing the name of the supporting organization and grant number.

• **Abbreviations**. The full term for which an abbreviation stands should precede its first use in the text unless it is a standard unit of measurement.

• **Trade names.** Generic terms are to be used when ever possible, but trade names and manufacturer should be included parenthetically at first mention.
• **Clinical Relevance**. Please include a very brief (2 sentences or 3 lines) clinical relevance statement.

REFERENCES

• **All references must be cited** in the text, according to the alphabetical and numerical reference list.
• **The reference list** should appear at the end of the article, in alphabetical and numerical sequence.
• **Do not include unpublished data** or personal communications in the reference list. Cite such references parenthetically in the text and include a date.
• **Avoid using abstracts** as references.
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1. Hannam AG, Langenbach GEJ, Peck CC. Computer simulations of jaw biomechanics. In: McNeill C (ed). Science and Practice of Occlusion. Chicago: Quintessence, 1997:187-194.

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