



Contents lists available at ScienceDirect

Saudi Journal of Biological Sciences

journal homepage: www.sciencedirect.com

Original article

Silver diamine fluoride with delayed restoration reduces tooth discoloration

Eman Alsagob, Nozha Sawan, Shahad Aladhyan, Nouf Alsalem, Abeer Alshami*, Sarah Albluwi

Preventive Dental Sciences Department, College of Dentistry, Princess Nourah Bint Abdulrahman University, Riyadh 11564, Saudi Arabia

ARTICLE INFO

Article history:

Received 20 October 2021

Revised 15 November 2021

Accepted 17 November 2021

Available online 1 December 2021

Keywords:

Caries

Silver diamine fluoride

Tooth discoloration

Dental restoration

Glass ionomer cements

ABSTRACT

Introduction: The standard treatment for caries is to apply silver diamine fluoride (SDF) to the tooth, followed by a composite resin or glass ionomer cement restoration (GIC). Tooth discoloration is an adverse effect of SDF. The aims of this study were to (1) determine whether applying a composite compared to a GIC restoration after SDF to caries-infected teeth results in less discoloration, and (2) determine whether immediate or delayed restoration application is associated with less discoloration.

Methods: Sixty samples of caries-infected teeth were divided into five groups: (1) control (SDF alone), (2) SDF plus immediate composite restoration, (3) SDF plus immediate GIC restoration, (4) SDF plus delayed composite restoration, and (5) SDF plus delayed GIC restoration. The delay between SDF and restoration for groups 4 and 5 was two weeks. Tooth color was measured at three sites for each sample at baseline before SDF application and at multiple times.

Results: When comparing the change between baseline color to the color at the last time measurement in all groups, we found that Group 4 (17.4 ± 4.3) and Group 5 (14.4 ± 5.3) changed the least compared to baseline and were not statistically significantly different from each other.

Conclusion: Under laboratory conditions, delaying application of restoration for two weeks after SDF to samples of caries-infected teeth significantly reduced discoloration, with neither composite nor GIC being superior. If these findings are confirmed in a clinical setting, delaying restoration by two weeks could provide an inexpensive oral health strategy to reduce the negative aesthetic impact associated with SDF.

© 2021 Published by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Dental caries is a prevalent chronic disease worldwide (Selwitz et al., 2007; Meyer and Enax, 2018). Historically, emphasis has been placed on treatment rather than prevention (Selwitz et al., 2007). This is unfortunate because the successful treatment involves restoration, which has drawbacks, including low durability and the tendency for caries to reoccur at the margins (Selwitz et al., 2007; Zhao et al., 2017).

* Corresponding author at: Preventive Dental Sciences Department, College of Dentistry, Princess Nourah Bint Abdulrahman University, Airport Road, Riyadh 11564, Saudi Arabia.

E-mail address: aaalshami@pnu.edu.sa (A. Alshami).

Peer review under responsibility of King Saud University.



The lack of emphasis on prevention has a disproportionate impact on children. Epidemiological estimates of the prevalence of pediatric caries are as high as 50% in Australia, almost 90% in Qatar, and 36% in Greece (Meyer and Enax, 2018). Fortunately, silver diamine fluoride (SDF) is now a low-cost and safe solution that can be applied to arrest the progression of caries (Gao et al., 2016; Zhao et al., 2018; Garg et al., 2019). The SDF is first applied to stop caries, then the restoration is applied, which can be developed from amalgam, resin composite or glass ionomer cement (GIC) (Zhao et al., 2017).

The authors of a systematic review and meta-analysis of clinical trials of SDF application before restoration in children with caries reported that SDF application arrested 81% of caries (95% confidence interval [CI] 68–89%) (Gao et al., 2016). They also found that there were no complications of SDF use except that it stained the affected lesion black, which is unaesthetic (Gao et al., 2016; Garg et al., 2019).

The stain results from SDF reacting with elements in the air, and this downside has led to tests of various strategies to reduce tooth discoloration without impacting the caries-arresting effect. These approaches include using an application of potassium iodide (KI)

to slow discoloration (Zhao et al., 2017; Garg et al., 2019), as well as applying bleach to lighten the discoloration (Horst et al., 2016). Ultimately, these are not recommended, as they have unclear aesthetic benefits and they interfere with the action of the SDF (Horst et al., 2016). According to the University of California San Francisco (UCSF) protocol, it is important to communicate the aesthetic impact of SDF use to the patient during consent, as this staining effect elicits most of the resistance to SDF use (Horst et al., 2016). In one study, one-third of parents rejected SDF treatment for caries in their child based on aesthetic concerns (Crystal et al., 2017).

In the search for strategies to reduce tooth staining caused by SDF, less-explored alternatives to the co-application of other substances include adjusting the timing of restoration application and the type of restoration applied. The objectives of this laboratory study were to (1) determine whether applying a composite vs. a GIC restoration after SDF application to caries-infected teeth results in less staining, and (2) determine whether immediate vs. delayed application of the restoration is associated with less staining. It was hypothesized that there would be no colour change using any of the treatment methods.

2. Methods

2.1. Materials used

The precision cutter was Isomet 1000 (Buehler, Lake Bluff, IL, USA) with a low concentration diamond saw (15LC, Buehler, Lake Bluff, IL, USA). The mounting resin was self-cure orthodontic resin (Techno Sin Resin, ProTechno, Vilamilla, Spain). The cylinder was polyvinyl chloride (PVC). We used 38% SDF liquid (Advantage Arrest, Elevate Oral Care, West Palm Beach, FL, USA), which was the optimal concentration based on the systematic review (Gao et al., 2016). To standardize the thickness of restorations, we used a polyvinyl siloxane (PVS) mold. In the composite restorations, we used 37% phosphoric acid etching gel 37% (Scotchbond Universal Etchant, 3 M, Maplewood, MN, USA) and adhesive (Scotchbond University Adhesive ESPE, 3 M, Maplewood, MN, USA). Light-curing was done with Bluephase N MC, which is a mains-operated LED polymerization light with a light intensity of 800 MW/cm². The resin composite restoration we used was shade A2 Clearfil Majesty (Kuraray, NY, USA), and the self-cured GIC restorative material we used was shade A2 Ketac Fil Plus Aplicap (3 M, Maplewood, MN, USA). Color measurements were performed using LabScan XE spectrophotometer, 0°/45° optical geometry (HunterLab, Reston, VA, USA). Data were analyzed using R (R Core Team, R, 2020).

2.2. Study design

This was a laboratory study of 30 caries-affected teeth sectioned into 60 samples divided across five groups. One group served as the control group and was only treated with SDF. The other four groups received one of two restorations (composite vs. GIC) applied on one of two schedules (immediately after SDF application vs. delayed by two weeks after SDF application). The discoloration was measured at several time points throughout the study. The following sections describe the sample preparation, color measurement, and data analysis. This study was approved by the Institutional Review Board (IRB) of Princess Nourah bint Abdulrahman University (PNU).

2.3. Sample preparation

Thirty posterior permanent teeth with cavitated carious lesions and an International Caries Detection and Assessment Score

(ICDAS) of five were extracted from patients in the dental clinic at PNU College of Dentistry (CoD) (Melgar et al., 2016). Each tooth was sectioned into two parts using the precision cutter and low concentration diamond saw under constant irrigation, yielding 60 samples.

2.4. Experimental groups

The 60 samples were divided into five groups. Group 1, control, included 20 samples that received SDF at baseline only with no follow-up restoration. These were measured at several time points throughout the study. This group represented the natural discoloration resulting from SDF application with no follow-up restoration.

Groups 2 and 3 included 10 samples each. Like Group 1, SDF was applied at baseline. In addition, Group 2 received a subsequent immediate application of the composite restoration, and Group 3 received a subsequent immediate application of the GIC restoration. Like with Group 1, Groups 2 and 3 were measured for discoloration at several time points throughout the study. Groups 2 and 3 represent the discoloration that would be expected to be observed under current standard clinical care using these restorations.

As with Groups 2 and 3, Groups 4 and 5 included 10 samples each. Group 4 received a composite restoration whereas Group 5 received a GIC restoration after the SDF application. However, unlike Groups 2 and 3, these restorations were applied two weeks after the SDF was applied at baseline. These groups represent an alternative schedule to current clinical care for applying restorations. As with the other groups, Groups 4 and 5 were also measured for discoloration at several time points throughout the study.

2.5. Procedures

First, all samples were treated with SDF. Samples were mounted using self-cure orthodontic resin within a PVC cylinder to ensure that the full carious lesion was visible. Then, SDF was applied to the carious lesion with a micro brush for one to two minutes.

Following this SDF application, the 20 samples in Group 1 did not receive any other treatments. Groups 2, 3, 4, and 5 were subsequently restored in distilled water. To ensure a standardized thickness for all restorations, we developed a custom PVS mold for each sample receiving a restoration; the mold provided 2 mm in height by 5 mm diameter restoration cylinders.

Samples in Groups 2 and 4 were treated with composite restorations on two different schedules. To apply the composite restorations, first, 27% phosphoric acid etching gel was applied to each sample for 20 s, then each sample was washed and dried. The adhesive was then applied with a micro brush and light-cured using the polymerization light, and the composite restoration was applied incrementally within the PVS mold, then light-cured for 40 s. Samples in Groups 3 and 5 were treated with GIC restorations on two different schedules. To apply the GIC restorations, self-cured GIC material was applied incrementally within the PVS mold (using the same approach as with the composite restorations).

2.6. Color measurement

Color measurements were obtained at standardized time points during the study. Baseline (BL) refers to the time before any application of SDF, and T1 refers to the time immediately after SDF application. The color was measured at BL and T1 for all samples. For Groups 2 and 3, restorations were immediately applied; T2 refers to the time after these restorations were applied. Therefore, only Groups 2 and 3 have a color measurement at T2. T3 refers to

two weeks after BL. For Groups 1, 2, and 3, a color measurement was obtained at T3. For Groups 4 and 5, restorations were applied at T3, but color measurements were not taken (due to the COVID-19 shutdown of the laboratory). T4 refers to four weeks after BL, and all groups were measured at T4. Each time color was measured, a total of three measurements were taken, each at a different site on the sample.

The color measurement was obtained using the CIELAB color space, in which each color is mapped onto a three-dimensional space. The CIELAB measurement consists of three values: L* (representing lightness), the a* axis (representing the red-green component), and the b* axis (representing the blue-yellow component) (Luo et al., 2001). A formula, called the Δ E 2000, was developed to calculate the absolute difference between the colors measured using this method. The formula produces a value

between 0 and 100, where 0 represents identical color, and 100 represents the opposite color (Luo et al., 2001; Davis, 2020). As this is a standard approach in dental research for studying tooth discoloration, the Δ E 2000 formula was used to calculate differences between BL and T4 for all groups (Paul et al., 2002; Sayed et al., 2019).

2.7. Data analysis

To calculate Δ E 2000 between BL and each measured time point for all groups, we used the R package spaces XYZ (Davis, 2020). First, the Δ E was calculated for each of the three measured sites on the sample at each time point, then these measurements were averaged together to represent the Δ E measurement for that sample at each time point. To test the null hypothesis that all mean

Table 1
Mean Δ E 2000 between baseline measurement and measurement at each time period by group.

Group Code	Group Description	Δ E (BL, T1) mean, sd	Δ E (BL, T2) mean, sd	Δ E (BL, T3) mean, sd	Δ E (BL, T4) mean, sd**	Number of Samples
1	Control	24.2, 9.6	NA	41.7, 7.3	41.3, 7.1 ^{a,b}	20
2	SDF only Composite	19.0, 8.8	16.2, 8.8	26.0, 5.8	29.3, 5.4 ^a	10
3	Immediate application GIC	22.8, 8.7	15.3, 8.8	13.8, 9.8	45.2, 7.2 ^b	10
4	Immediate application Composite	28.0, 7.5	NA	NA*	17.4, 4.3 ^c	10
5	Delayed application GIC	29.7, 8.3	NA	NA*	14.4, 5.3 ^c	10

NA = Not applicable due to lack of measurement, Δ E = Δ E 2000 measurement, GIC = glass ionomer cement, SD = standard deviation. For times, BL = Baseline, before application of silver diamine fluoride (SDF) for all groups, T1 = after application of SDF at baseline for all groups, T2 = after application of either composite (Group 2) or GIC (Group 3) after SDF application at baseline (and NA for all other groups), T3 = two weeks after baseline for Groups 1, 2, and 3 (and NA for Groups 4 and 5), and T4 = 4 weeks after baseline for all groups. *Composite (Group 4) and GIC (Group 5) applied at T3, but COVID-19-related closures precluded taking measurements at this time. ** Pairwise t-test results using Bonferroni correction: ^a indicates that mean BL to T4 Δ E 2000 for Groups 1 and 2 were not statistically significantly different, ^b indicates Groups 1 and 3 were not statistically significantly different, and ^c indicates Groups 4 and 5 were not statistically significantly different.

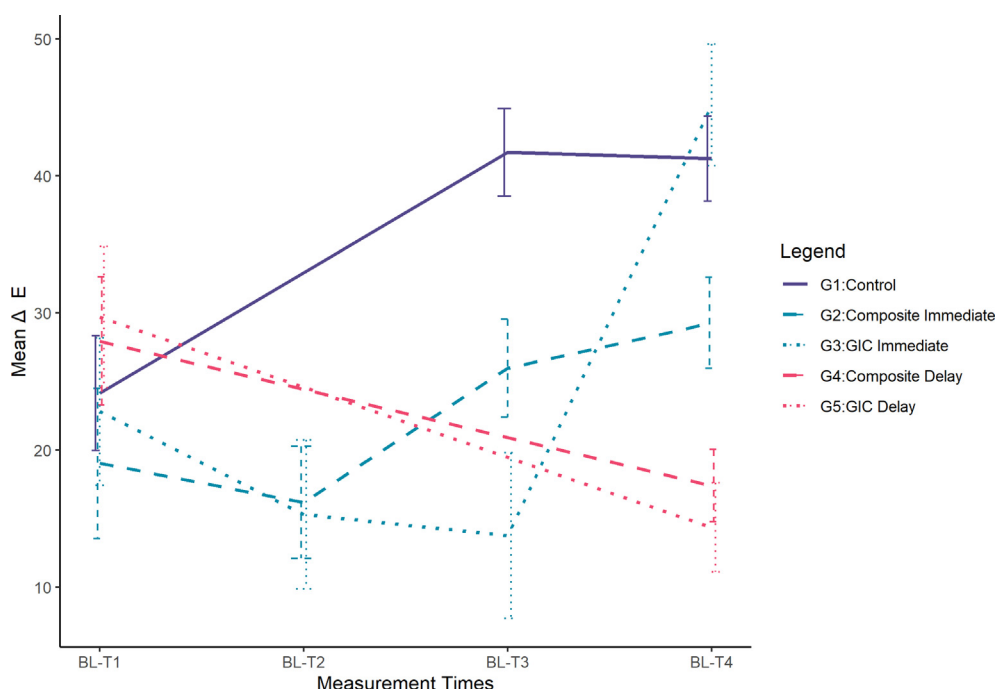


Fig. 1. Mean Δ E 2000 between baseline measurements and measurements at each time period by a group. Δ E = Δ E 2000. Error bars represent 95% confidence intervals. G1–G4 = Groups 1–4, GIC = glass ionomer cement. For times, BL = Baseline, before application of silver diamine fluoride (SDF) for all groups, T1 = after application of SDF at baseline for all groups, T2 = after application of either composite (Group 2) or GIC (Group 3) after SDF application at baseline (and NA for all other groups), T3 = two weeks after baseline for Groups 1, 2 and 3 (and NA for Groups 4 and 5), and T4 = 4 weeks after baseline for all groups.

BL to T4 ΔE 's were not statistically significantly different from one another, an analysis of variance (ANOVA) (Khan et al., 2019) was conducted with the BL to T4 ΔE as the dependent variable, group as the independent variable and $\alpha = 0.05$. In the case of statistical significance, pairwise t-tests with Bonferroni correction (Alharbi et al., 2014) were applied.

Finally, to better understand the trajectory of discoloration in each group over time, mean ΔE 's for BL vs. each measured time point were visualized in a time series chart. To aid interpretation, 95% confidence intervals were calculated at each time point and included in the chart as error bars.

3. Results

The means and standard deviations (SDs) for ΔE 2000 between BL and each measured time point for all groups are presented in Table 1.

The ANOVA for the ΔE 2000 between BL and T4 was statistically significant ($F = 47.8$ at 49 df, $p < 0.0001$), so pairwise t-tests between groups were conducted. As shown in Table 1, the color change from BL to T4 was statistically significantly lower in Groups 4 and 5 (mean ΔE 2000 17.4 and 14.4, respectively) compared with Groups 1, 2, and 3 (mean ΔE 2000 41.3, 29.3, and 45.2, respectively). Fig. 1 shows the trajectory of the color change throughout the follow-up period.

Consistent with the ANOVA and t-test results, at T4, Groups 4 and 5 showed the least change in color from BL, and neither Group 4 nor Group 5 showed statistical superiority in lack of color change from BL to T4.

4. Discussion

The results showed that composite resin and GIC restorations performed similarly concerning discoloration when used after SDF application in caries-infected teeth. When applied immediately after SDF, the composite restoration performed slightly better than GIC. However, when restorations were applied two weeks after SDF application, both performed similarly and resulted in the least amount of discoloration from baseline. The mean ΔE 2000's for BL to T4 measurements in the composite and GIC groups were 17.4 and 14.4, respectively, which is consistent with staining results in a similarly-designed laboratory study of dentin discoloration due to SDF application, demonstrating clinical significance in terms of preservation of aesthetics (Sayed et al., 2019).

These findings suggest that this timing variation is a viable approach to reducing discoloration after SDF application in caries patients without reducing SDF's caries-arresting effects. However, in order to be validated, these findings would need to be replicated in actual patients. Currently, there are no particular recommendations regarding the timing of restoration application after SDF. Current American Dental Association (ADA) clinical practice guidelines on nonrestorative treatments for carious lesions include the application of 38% SDF and note that these are often used in conjunction with restorative treatments, but do not recommend specific restorations or timing (Slayton et al., 2018).

In pediatric patients, the main concern with applying SDF two weeks before restorations would be that the anti-caries action of the SDF would be disrupted. Further, it is unclear what impact routine exposures of food, saliva, and oral hygiene products to the caries lesion would have in the two weeks between the SDF application and restoration. If these laboratory results are replicated in the field, the clinical guidelines should be updated to include this delay between the application of SDF and restoration. An additional practical concern is that requiring two appointments

runs the risk that the second procedure – the restoration – will not occur. The logistics of two appointments as opposed to one are also complicated by the risks posed specifically in pediatric dentistry by the COVID-19 pandemic (Al-Halabi et al., 2020).

5. Conclusion

In this laboratory study, delaying the application of restoration after SDF by two weeks resulted in significantly less discoloration of caries-infected teeth compared to immediate restoration application. Future studies should examine the efficacy of this restoration schedule in clinical populations and the feasibility of using this approach to reduce SDF-related tooth discoloration in pediatric caries patients.

Declaration of Competing Interest

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

Acknowledgments

This research was funded by Princess Nourah bint Abdulrahman University Researchers Supporting Project number (PNURSP2022R202, princess Nourah bint Abdulrahman University ,Riyadh,Saudi Arabia.

References

- Al-Halabi, M., Salami, A., Alnuaimi, E., Kowash, M., Hussein, I., 2020. Assessment of paediatric dental guidelines and caries management alternatives in the post COVID-19 period. A critical review and clinical recommendations. *Eur Arch Paediatr Dent*, 1–14.
- Alharbi, K.K., Khan, I.A., Munshi, A., Alharbi, F.K., Al-Sheikh, Y., Alnbaheen, M.S., 2014. Association of the genetic variants of insulin receptor substrate 1 (Irs-1) with type 2 diabetes mellitus in a Saudi population. *Endocrine* 47 (2), 472–477.
- Crystal, Y.O., Janal, M.N., Hamilton, D.S., Niederman, R., 2017. Parental perceptions and acceptance of silver diamine fluoride staining. *J Am Dent Assoc* 148 (7), 510–518.e4.
- Davis, G., 2020. spacesXYZ: CIE XYZ and Some of its Derived Color Spaces [Internet] [cited 2020 Nov 28]. Available from: <https://CRAN.R-project.org/package=spacesXYZ>.
- Gao, S.S., Zhao, I.S., Hiraishi, N., Duangthip, D., Mei, M.L., Lo, E.C.M., Chu, C.H., 2016. Clinical trials of silver diamine fluoride in arresting caries among children: a systematic review. *JDR Clin Transl Res* 1 (3), 201–210.
- Garg, S., Sadr, A., Chan, D., 2019 Jun. Potassium iodide reversal of silver diamine fluoride staining: a case report. *Oper Dent* 44 (3), 221–226.
- Horst, J.A., Ellenikiotis, H., Milgrom, P.M., 2016 Jan. UCSF protocol for caries arrest using Silver diamine fluoride: rationale, indications, and consent. *J Calif Dent Assoc* 44 (1), 16–28.
- Khan, I.A., Jahan, P., Hasan, Q., Rao, P., 2019. Genetic confirmation of T2dm meta-analysis variants studied in gestational diabetes mellitus in an Indian population. *DiabetesMetab Syndr* 13 (1), 688–694.
- Luo, M.R., Cui, G., Rigg, B., 2001. The development of the CIE 2000 colour-difference formula: CIEDE2000. *Color Res Appl* 26 (5), 340–350.
- Melgar, R.A., Pereira, J.T., Luz, P.B., Hugo, F.N., Araujo, F.B.d., 2016. Differential impacts of caries classification in children and adults: a comparison of ICDAS and DMF-T. *Braz Dent J* 27 (6), 761–766.
- Meyer, F., Enax, J., 2018. Early childhood caries: epidemiology, aetiology, and prevention [Internet] *Int J Dent* 2018, 1–7.
- Paul, S., Peter, A., Pietrobon, N., Hämmerle, C.H.F., 2002. Visual and spectrophotometric shade analysis of human teeth. *J Dent Res* 81 (8), 578–582.
- R Core Team, 2020. R: A Language and Environment for Statistical Computing. [Internet]. Vienna, Austria: R Foundation for Statistical Computing. Available from: <https://www.R-project.org/>.
- Sayed, M., Matsui, N., Hiraishi, N., Inoue, G., Nikaido, T., Burrow, M.F., et al., 2019 Feb 8. Evaluation of discoloration of sound/demineralized root dentin with silver diamine fluoride: in-vitro study. *Dent Mater J* 38 (1), 143–149.
- Selwitz, R.H., Ismail, A.I., Pitts, N.B., 2007. Dental caries. *Lancet* 369 (9555), 51–59.
- Slayton, R.L., Urquhart, O., Araujo, M.W.B., Fontana, M., Guzmán-Armstrong, S., Nascimento, M.M., Nový, B.B., Tinanoff, N., Weyant, R.J., Wolff, M.S., Young, D.A., Zero, D.T., Tampi, M.P., Pilcher, L., Banfield, L., Carrasco-Labra, A., 2018. Evidence-based clinical practice guideline on nonrestorative treatments for

- carious lesions: a report from the American Dental Association. *J Am Dent Assoc* 149 (10), 837–849.e19.
- Zhao, I.S., Mei, M.L., Burrow, M.F., Lo, E.-C.-M., Chu, C.-H., 2017. Effect of silver diamine fluoride and potassium iodide treatment on secondary caries prevention and tooth discolouration in cervical glass ionomer cement restoration. *Int J Mol Sci* 18 (2) [Internet] Feb 6 [cited 2020 Nov 27] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5343875/>.
- Zhao, I.S., Gao, S.S., Hiraishi, N., Burrow, M.F., Duangthip, D., Mei, M.L., Lo, E.-M., Chu, C.-H., 2018. Mechanisms of silver diamine fluoride on arresting caries: a literature review. *Int Dent J* 68 (2), 67–76.