The protective effect of topical fluoride treatments in dentine lesions

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Chapter 8

Summary
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Non restorative cavity control (NRCC) is a non to minimally invasive dental approach in dentine caries management which can be applied to cavitated dentine lesions in the primary and permanent dentition. This approach could be supported by topical fluoride applications to enhance caries arrestment. Caries arrestment is a clinical sign of the success of the NRCC approach. The subject of the current thesis is to understand more closely the chemical and histological (microradiographic) aspects of this arrestment. Therefore, this thesis has investigated these aspects in dentine lesions after treatment with various topically applied fluoride products (SDF, NaF, TiF$_4$, and SnF$_2$). The aim was to examine the effects of these products on demineralized dentine lesions and to study which product performs the best in dentine caries arrestment in an in vitro de- and remineralization model. This could inform the dental care professionals to decide which product is favorable to use in treating cavitated dentine lesions.

This thesis started with comparing the interaction between various fluoride products and demineralized dentine lesions under constant remineralization conditions (Chapter 2). Therefore, specimens of demineralized dentine lesions had been treated once either by SDF solution (35,400 ppm F), NaF varnish (22,600 ppm F), TiF$_4$ solution (9,180 ppm F), SnF$_2$ gel (1,000 ppm F) or received no treatment (control group). Part of the specimens was examined using scanning electron microscopy (SEM) and the remaining specimens were immersed separately in a remineralization buffer for fourteen days. After completion of the remineralization period, the experimental specimens were histologically analyzed using transversal microradiography (TMR). The SEM pictures showed crystal-like deposits only on the surfaces of the dentine lesions treated with SDF and TiF$_4$. Post experimental TMR analysis showed remineralization in all groups, with no significant differences in ΔIML between these groups. However, differences in the patterns of mineral deposition were observed. SDF enhanced mineral deposition on the surface of the dentine lesions, while mineral was lost from the surface of the dentine lesions and deposited mainly in the body of the lesion after application of TiF$_4$. These findings revealed that the selected fluoride products interacted differently with demineralized dentine lesions, indicating probable differences in the protection mechanism of those products. Therefore, further studies were indicated to be conducted under more realistic conditions.

In Chapter 3 the same fluoride products were used but now under de- and remineralization conditions (pH-cycling model). Artificially demineralized dentine lesions were treated once with SDF, NaF, TiF$_4$, SnF$_2$, or no treatment (control), and then subjected to 15 days of pH-cycling. The chemical data of the de- and remineralization buffers: daily calcium analysis and fluoride measurements on day 1, 2, 3, 5, 8, 13 were collected. The separate cycles of
de- and remineralization revealed differences in the effect of the applied fluoride products. In the demineralization cycle, TiF$_4$ revealed a significant reduction of demineralization compared to the other experimental groups. In the remineralization cycle, SDF enhanced remineralization significantly higher than the other groups. The combined data of both cycles disclosed a significant inhibition of dentine demineralization in dentine lesions treated with SDF followed by TiF$_4$ > NaF > SnF$_2$. Further demineralization was observed in the control group in both de- and remineralization cycles. The effect of the fluoride products in the cycles of de- and remineralization was constant throughout the whole period of 15 days pH-cycling. The fluoride measurements in de- and remineralization revealed a steep reduction in fluoride release over time. These two findings, constant inhibition and pattern of fluoride release disclosed that fluoride released in the buffers did not contribute to the process of inhibiting demineralization or enhancing remineralization. In conclusion, all fluoride products could significantly inhibit the demineralization of the dentine lesion. SDF showed a net superior effect compared to the other experimental groups. We assumed that the continuous constant effect of the fluoride products was attributed to the fluoridated mineral and not to the released fluoride in the de- and remineralization buffers. Therefore, studying the pattern and the amount of mineral deposition inside the dentine lesions is crucial to understand the fluoride effect in the dentine lesion layers and how this effect contributes to dentine remineralization.

In Chapter 4 the histological data of Chapter 3 are presented. The mineral distribution profiles and ∆IML in dentine lesions treated with SDF, NaF, TiF$_4$, SnF$_2$ or no treatment (control) are analyzed using TMR. The intersection points (IP) between the mineral distribution profiles of the baseline lesion and the experimental groups divided the lesion profiles into two parts; the outer (zone 1) and the deeper part (zone 2). The intersection points represent the transmission area from net mineral gain to net mineral loss. The depth of the intersection points differed between the groups where the depth was comparable in SDF and TiF$_4$ but less deeper in NaF and SnF$_2$. The mineral distribution profiles showed remineralization in the outer part and body of the lesion, but further demineralization of the inner part of the lesion was observed in all fluoride groups. However, SDF group showed a significant hyper-remineralization in zone 1 and revealed the development of the smallest secondary lesion among the other groups in zone 2. ∆IML showed significant remineralization in zone 1 of dentine lesions treated with fluorides compared to the control group that showed demineralization. SDF disclosed significant remineralization among the other fluoride groups in that zone. However, all experimental groups showed demineralization in zone 2. An additional experiment was performed on the sides of the pH-cycled specimens as a perpendicular exposure for 12 h. After completion of the 12 h of perpendicular acid exposure, significant remineralization was observed in zone 1 of the dentine lesions treated with SDF. Differently, further demineralization was observed.
in dentine lesions treated with NaF, TiF₄, and SnF₂ with no significant difference from the control group in zone 1. However, all experimental groups showed further demineralization in zone 2 and the sound dentine zone. These findings indicated that SDF is effective in enhancing the dentine remineralization and protecting against further demineralization to some extent. More studies are needed to interpret the possible reasons for the significant effect of SDF in dentine caries development. We assumed that the superior effect of SDF was perhaps attributed to its high fluoride concentration, which is the highest among all topical fluoride products used in the dental office. In addition, it was of interest to find out whether the silver component participated in the anti-demineralizing and remineralizing promoting activity of the SDF.

For those reasons, the experiments in Chapter 5 and 6 were designed to compare SDF to another fluoride treatment which has the same fluoride concentration as SDF. This was to estimate the effect of the high fluoride concentration in SDF, as well as to investigate whether silver played a role in the anti-demineralizing/remineralizing promoting activity of SDF. Thus, Chapter 5 was aimed to compare the chemical data (calcium and fluoride analysis) of three different fluoride concentrations (4.1%, 1.025%, 0.26%) either as SDF or KF on dentine lesions. Dentine lesions were treated once with the three fluoride concentrations of SDF, KF, or no treatment (control), and then subjected to 15 days of non-microbial pH-cycling. The daily calcium loss and uptake in the de- and remineralization buffers were analyzed. The fluoride release into the de- and remineralization buffers was analyzed on days 1, 2, 3, and 8. In the demineralization cycle, significant inhibition of demineralization was observed in dentine lesions treated with KF (4.1%F⁻). In the remineralization cycle, and regardless of the type of fluoride, significant enhancement of remineralization was observed in all fluoride groups compared to the control group. The net data of both cycles showed a significant dose response relationship between the fluoride concentrations, but there was no difference between the fluoride compounds. A constant daily effect of the fluoride treatments was found throughout the whole period of pH-cycling. A significant amount of fluoride release was observed only on the first day of the experiment. This finding indicated that the released fluoride into the surrounding buffers did not contribute to the constant effect of the fluoride treatments throughout the whole period of the experiment, indicating that the constant effect is attributed more to the fluoridated mineral. These findings revealed that there is no difference in the effectiveness of SDF and KF with the same fluoride concentrations when both treatments were applied to dentine lesions.

In Chapter 6, the histological (microradiographic) data of the experiment described in Chapter 5 was investigated. Mineral distribution and content in the dentine lesions treated with the three concentrations of either SDF or KF, as well as the no treatment group (control) were examined using transversal microradiography (TMR). A subsequent experiment using
scanning electron microscopy (SEM) was conducted to examine the surface morphology and the cross sections of dentine lesions treated with SDF or KF (4.1%F), or no treatment (control). Some of these specimens were treated with fluorides and then pH-cycled for 21 days before SEM examination, while the remaining specimens were examined with SEM immediately after the fluoride applications. Moreover, an energy-dispersive X-ray (EDS) was performed to examine the chemical composition of the anticipated deposits on the dentine lesions treated with SDF. TMR profiles showed mineral deposition throughout the dentine lesions treated with fluorides. The ΔIML data showed demineralization in the dentine lesions treated either with SDF of KF of 0.26%F, which was not significantly different from the control group. Significant remineralization was observed in dentine lesions treated either with SDF or KF of 4.1%F and less with 1.025%F. SEM examination revealed distinct deposits on the surface of the dentine lesions treated with SDF and not subjected to pH-cycling. The deposits were also detected in the cross sections of the dentine lesions treated with SDF at the depths of 150 and 300 μm. EDS analysis disclosed that these deposits composed of high atomic ratio of silver. Under the chosen conditions, we conclude that there is no difference in the amount of mineral deposition between SDF and KF, neither in the effectiveness between both treatments in inhibiting demineralization or enhancing remineralization of the dentine lesions. Despite the amount of silver deposition on the surface and in the dentinal tubules of the lesions treated with SDF, these deposits could not enhance the mineral deposition or remineralization better than in the KF groups. Based on the current findings, we conclude that the superior effect of the SDF compared to other fluoride products used in the dental office is attributed to its high fluoride concentration, while the presence of silver plays no role in the anti-demineralizing and remineralization promoting activity of SDF. The anti-microbial effect of silver was not in the scope of this thesis.

Based on the current findings, this thesis contributes to the understanding of the role of topical fluoride products in dentine caries management and so to explain the contribution of topical fluoride application on the success of the NRCC approach. It was clear that the effectiveness of the fluoride application to dentine lesions was dependent on the fluoride formulas and concentrations. It could be concluded that all fluoride products used in the current thesis were effective in inhibiting demineralization or enhancing remineralization, depending on the formulas and concentration of the product. This finding reflects the importance of usage of these products in treating cavitated dentine lesions. This thesis also revealed that SDF was the most effective product in dentine caries management, and it performed the best in dentine lesions repair compared to the other fluoride products. The high fluoride concentration of SDF was the probable reason for its significant effect on dentine lesions, while the silver component of SDF did not contribute to the process of inhibiting demineralization or enhancing remineralization.