Clinical effectiveness/child-patient and parent satisfaction of two topical fluoride treatments for caries: a randomised clinical trial

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Article

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Abstract

Knowledge gaps exist regarding optimal silver diammine fluoride (SDF) regimens and the efficacy of new products for arresting dental caries in young children. We evaluated the effectiveness of 38%-SDF(SDI-RivaStar), Tiefenfluorid(TF) comparing with Placebo(P), all in conjunction with behavioural modification(BM), in preventing major complications (endodontic/extractions/pain) —a patient-centred outcome— due to early childhood caries over 12 months in children under 71-months. A six-arm, patient/parent-blinded, superiority, placebo-controlled randomised control trial at the university clinic in Riga, Latvia, from 1/9/20-31/8/22 (Protocol registration ISRCTN17005348). The trial tested six protocols, using three compounds (P/SDF/TF) under two regimes: annual and biannual (P1/P2/TF1/TF2/SDF1/SDF2) for major complications. Secondary outcomes included minor complications and parental satisfaction. All groups received BM. 373/427 randomised children (87.3%) completed the study. SDF2 had a significantly lower rate and risk of major (21.5%, OR=0.28, 95%CI[0.11, 0.72], p<0.05) and minor complications (OR=0.16 (95%CI [0.05, 0.50], p=0.002). Overall satisfaction was 96%(p>0.05). SDF biannual application with BM effectively prevented major complications of early childhood caries and was well accepted by children and their parents. Trial registration number: ISRCTN17005348, principal investigator: Ilze Maldupa, registration date: 30/06/2021.

Introduction

Oral health is an essential element of general health and positively influences child development.[1] Caries develops as a result of behaviours, and complex evidence-based interventions are needed to prevent or manage it and halt further progress of the disease.[2] Non-invasive caries treatment strategies have been proposed. As well as being non-invasive, these have the additional advantage of lowering care costs and decreasing the number of tooth extractions[3]. Notably, silver diammine fluoride (SDF) has been found to have up to 89% higher efficacy than other treatments or placebos.[4,5] However its use is limited by its poor esthetic appearance. The optimal application frequency for SDF treatment remains unresolved, and there is a lack of research on the comparative effectiveness of different products.[6] Also, new formulations, such as Tiefenfluorid™ (TF), have gained significant traction in some countries such as Latvia, for their ability to remineralise teeth without the drawback of black staining, as demonstrated by *in vitro* studies. [7,8] However, clinical trials comparing existing and new formulations, are lacking.

Dental caries significantly affects children, causing pain, difficulty sleeping, loss of time from school and is expensive to treat[9]; however, research in dentistry has traditionally prioritised clinician-centred measures, such as arresting dental caries or preventing lesion progression[4,5,10,11] expressed numerically and neglecting patient-centred outcomes (PCOs).[12]

While it is widely acknowledged that childhood caries is linked to family behaviour [13] and that behaviour change is a complex process[14], family motivation is still seldom taken into account in clinical trials.[15] To promote the health and well-being of children beyond mechanical or restorative treatments, it is crucial to prioritise research that can help transfer evidence-based practices into real-world settings.[16] For scaling-up evidence-based interventions in national health systems[2] for the treatment of early childhood caries, there needs to be a more comprehensive understanding of fluoride compounds and their optimal use, combined with behaviour change interventions. These must be understood within the context of outcome measures expressed in PCOs.

This placebo-controlled randomised clinical trial, aimed to evaluate the effectiveness of two fluoride-containing products (SDF and Tiefenfluorid) and a placebo, using two different application protocols (annual/biannual) in children under 6 years old. All groups, including the placebo, received a behavioural management (BM) intervention as part of the treatment protocol, making it a complex intervention. Outcomes were measured at 12 months. The focus was effectiveness from a patient-centred perspective, defined through the primary outcome of the proportion of major complications (parents-declared dental pain, tooth extraction, or endodontic treatment in the last 12 months) and the secondary outcomes of effectiveness arresting carious lesions (minor complications), and parental and children's satisfaction (through three outcomes: 1) would the parent be happy to have that treatment again for the same child or another of their children; 2) parent satisfaction with appearance and 3) child satisfaction with appearance). The outcomes, although broken down, were designed as composite variables to capture important treatment outcomes for parents and children and ensure that our findings were patient-centred.

Results

Baseline characteristics

There were 432 children screened as eligible, and 427 enrolled, randomised, received treatment and included in the analyses. Each group comprised 70–72 children (Fig. 1) at the start of treatment and 57–66 at the final 12-month analysis giving 373 participants examined at the 12-month follow-up, a 13% attrition rate. The percentage of missing data was less than 5% and the missing values were found to be missing at random based on the MCAR test. See Table 1 for more details on the study groups' composition. Initially, imbalances were visually detected between groups regarding toothbrushing frequency, d1mft, d3mft, and active lesions, which could have caused a chance bias. To address this, we incorporated these variables into the linear adjustment using a regression model to mitigate the potential for bias. The interventions were delivered as planned without personalization or adaptation. The adherence to the intervention was over 70% for all groups (**Supplementary material, table S1)**.

Table 1
Baseline demographic characteristics and oral health-related behaviours of children in each study group.

	P1	P2	TF1	TF2	SDF1	SDF2	Overall
	(N = 70)	(N = 72)	(N = 70)	(N = 72)	(N = 71)	(N = 72)	(N = 427)
Age (months)							
Mean (SD)	48.0 (12.0)	46.3 (15.3)	45.3 (13.5)	45.3 (14.8)	44.8 (13.2)	44.7 (15.4)	45.7 (14.1)
Median [Min, Max]	49.0 [16.0, 71.0]	45.5 [5.00, 72.0]	44.0 [5.00, 72.0]	45.5 [6.00, 76.0]	44.0 [8.00, 69.0]	46.5 [7.00, 70.0]	46.0 [5.00, 76.0]
Gender							
Female	31 (44.3%)	35 (48.6%)	30 (42.9%)	28 (38.9%)	26 (36.6%)	28 (38.9%)	178 (41.7%)
Male	39 (55.7%)	37 (51.4%)	40 (57.1%)	44 (61.1%)	45 (63.4%)	44 (61.1%)	249 (58.3%)
Toothbrushing frequency							
Twice or more	23 (32.9%)	13 (18.1%)	13 (18.6%)	17 (23.6%)	15 (21.1%)	25 (34.7%)	106 (24.8%)
Every evening	29 (41.4%)	38 (52.8%)	35 (50.0%)	35 (48.6%)	39 (54.9%)	24 (33.3%)	200 (46.8%)
Less	18 (25.8%)	21 (29.2%)	22 (31.5%)	20 (27.8%)	17 (23.9%)	23 (31.9%)	121 (28.4%)
Toothpaste							
Fluoride free	0 (0%)	2 (2.8%)	1 (1.4%)	3 (4.2%)	3 (4.2%)	3 (4.2%)	12 (2.7%)
< 1000 ppm F	42 (60.0%)	45 (62.5%)	43 (61.4%)	35 (48.6%)	36 (50.7%)	40 (55.6%)	241 (56.3%)
1000–1500 ppm F	28 (40.0%)	25 (34.7%)	26 (37.1%)	34 (47.2%)	32 (45.1%)	29 (40.3%)	174 (40.7%)
Sweets daily							
Yes	59 (84.3%)	54 (75.0%)	63 (90.0%)	57 (79.2%)	63 (88.7%)	62 (86.1%)	358 (83.8%)
Sugary drinks daily							
Yes	47 (67.1%)	49 (68.1%)	47 (67.1%)	53 (73.6%)	54 (76.1%)	41 (56.9%)	291 (68.1%)
Visible plaque							
Yes	41 (58.6%)	51 (70.8%)	51 (72.9%)	35 (48.6%)	46 (64.8%)	51 (70.8%)	275 (64.4%)
d1mft†							
Mean (SD)	9.06 (4.73)	8.82 (4.99)	10.4 (4.94)	8.33 (4.29)	9.93 (4.31)	6.64 (4.59)	8.85 (4.78)
Median [Min, Max]	9.00 [1.00, 20.0]	8.00 [1.00, 20.0]	10.0 [1.00, 20.0]	8.00 [2.00, 20.0]	10.0 [2.00, 20.0]	6.00 [1.00, 20.0]	8.00 [1.00, 20.0]
d3mft‡							
Mean (SD)	6.46 (3.72)	6.85 (4.56)	7.60 (4.50)	5.68 (3.31)	7.55 (3.87)	5.36 (3.64)	6.58 (4.03)
Median [Min, Max]	6.00 [1.00, 18.0]	6.50 [1.00, 20.0]	6.00 [1.00, 20.0]	5.00 [1.00, 14.0]	7.00 [1.00, 18.0]	4.00 [1.00, 15.0]	6.00 [1.00, 20.0]
Active lesions at baseline							
Mean (SD)	7.33 (5.06)	6.56 (4.64)	9.17 (4.75)	6.40 (4.66)	8.72 (4.13)	5.60 (4.05)	7.28 (4.71)
Median [Min, Max]	6.00 [0, 20.0]	5.50 [0, 20.0]	8.50 [1.00, 20.0]	5.50 [0, 20.0]	8.00 [2.00, 20.0]	5.00 [0, 20.0]	6.00 [0, 20.0]

† d1mft = damaged (ICDAS = 1–6), missed and filled teeth ; ‡ d3mft = damaged (ICDAS = 3–6), missed and filled teeth

Primary Outcome

The proportion (standard deviation) of major complications in each group was: P1 = 48.3% (6.9), P2 = 49.2% (7.0), TF1 = 50.9% (7.1), TF2 = 53.0% (7.3), SDF1 = 45.5% (6.7) and SDF2 = 21.5% (4.6). The group SDF2 presented the lowest proportion of major complications, and this difference was significant with $X^2 = 17.659$, df = 5, p-value = 0.0034 compared to the P2. Figure 2-A presents the results for major and minor complications. The unadjusted analysis revealed a visual interaction between compound and frequency of application, suggesting the effectiveness of SDF2 in reducing major complications (**Supplementary material**, Fig. 1); therefore, a GLM-adjusted model was useed to confirm these findings. The GLM model included various predictors and covariates for potential clustering, as shown in Table 2. The model's baseline intercept for the P2 group was 3.16 (95%CI [1.61, 4.72], p < 0.001). The SDF2

intervention resulted in a significant reduction in the odds of major complications (OR = 0.28, 95%CI [0.11, 0.72]), while the other intervention groups did not show a significant difference compared to the placebo after adjusting for covariates (**Supplementary material, table S2**).

Table 2
Association between intervention groups and major and minor complications risk: odds ratios and 95% CI from the adjusted regression model.

	Major complications			Minor complications		
	OR†	95% CI†	p-value	OR†	95% CI†	p-value
Intervention						
P2 - Placebo single applications, twice per year	—	—		—	—	
P1 - Placebo one annual regime (four applications, one week apart)	1.08	0.46, 2.52	0.9	0.52	0.15, 1.84	0.3
SDF1 - SDF one annual regime (four applications, one week apart)	0.74	0.33, 1.67	0.5	0.34	0.10, 1.19	0.091
SDF2 - SDF single applications, twice per year	0.28	0.11, 0.72	0.008	0.17	0.05, 0.54	0.003
TF1 - Tiefenfluorid one annual regime (four applications, one week apart)	0.94	0.40, 2.19	0.9	0.76	0.19, 3.01	0.7
TF2 - Tiefenfluorid single applications, twice per year	1.96	0.86, 4.44	0.1	0.58	0.18, 1.88	0.4
† OR = Odds Ratio, CI = Confidence Interval.						

Secondary Outcomes

For minor complications, there was no evidence of a difference in the proportion of minor complications **(**Fig. 2-B**)** across the different intervention groups (X^2 = 7.0725, df = 5, p = 0.2142). A mixed logistic model was used to predict minimal complications with fixed effects for covariates and a random effect of patients. The model's marginal R^2 related to the fixed effects was 0.46. SDF2 significantly reduced the risk of minimal complications, with an odds ratio of 0.16 (95%CI [0.05, 0.50], p = 0.002). The effects of interventions P1, TF1, TF2, and SDF1 were statistically non-significant. The details are presented in Table 2.

Regarding future treatment for the same or another child, most parents (96%) across all study groups reported that they would choose non-invasive caries management methods (Fig. 3A). There were 92.5% of parents and 94% of children who reported satisfaction with the treatment's aesthetic outcome and the appearance of their teeth, respectively (Figs. 3B and 3C). A regression model was used to predict parental satisfaction but had low explanatory power (Tjur's R^2 = 0.10) and found no significant differences between groups, as shown in Table 3. The absence of visible plaque was a significant factor in parental satisfaction with the aesthetic outcome (**Supplementary material, table S3**). The parents reported no adverse effects beyond the collected outcome measures.

Table 3
Association between intervention groups and parental satisfaction: odds ratios and 95% CI from the adjusted regression model.

	OR†	95% CI†	p-value
Intervention			
P2 - Placebo single applications, twice per year	—	—	
P1 - Placebo one annual regime (four applications, one week apart)	1.19	0.52, 2.77	0.7
SDF1 - SDF one annual regime (four applications, one week apart)	0.57	0.26, 1.22	0.2
SDF2 - ADF single applications, twice per year	1.12	0.49, 2.56	0.8
TF1 - Tiefenfluorid one annual regime (four applications, one week apart)	0.96	0.43, 2.15	> 0.9
TF2 - Tiefenfluorid single applications, twice per year	1.65	0.71, 3.90	0.2
† OR = Odds Ratio, CI = Confidence Interval.			

Discussion

In this study, we aimed to investigate the effects of non-invasive caries management interventions based around silver diammine fluoride, on a set of PCOs, namely major and minor complications, as well as child patient and parent satisfaction. We found that the biannual SDF application significantly reduced the odds of major complications by 20% (95%CI [11%, 72%], p < 0.001), while the other interventions, including SDF annually, did not show a significant difference compared to the placebo. SDF-biannually also substantially reduced the likelihood of minor complications by 84% (95%CI [50%, 95%], p = 0.002). Almost all parents (96%) from all study groups reported they would choose non-invasive caries management methods in the future. In terms of satisfaction, the effects of the different interventions were not statistically significant.

This clinical trial has limitations, such as potential performance bias due to unblinded operators and a single institution setting, which may limit generalisability. However, using PCOs, including major complications (comprising pain, need for endodontic treatment or tooth extraction), and child and parent satisfaction, provide valuable information on the acceptability and impact of interventions. PCOs are important for assessing treatments' effectiveness, relevance, and impact on patients, ensuring their appropriateness and a more satisfying experience. The raw data is available[17] and might enable future individual patient data meta-analyses.

Silver diammine fluoride (SDF) has gained interest as a minimally invasive treatment for dental caries. Clinical studies evaluating its efficacy have mainly focused on technical outcomes, such as arresting caries progression and preserving tooth structure with high dentine caries arrest rates being found consistently.[5,10,18,] Seifo et al.[6] conducted an umbrella review of 11 systematic reviews and found that SDF effectively prevented and arrested coronal carious lesions in primary and permanent teeth. For lesion arrest rate, it outperformed fluoride varnish, glass ionomer cement, and Atraumatic Restorative Treatment. The main side effect was black staining of the carious lesions. Although technical outcomes are important, PCOs are what matters to patients and often go uninvestigated and unreported. Therefore, our study investigated the effects of non-invasive caries management interventions on outcomes such as major and minor complications, patient and parent satisfaction, and technical outcomes. We found high child-patient and parent satisfaction with SDF, which aligns with previous studies.[19] A network meta-analysis found no differences in oral health-related quality of life (OHRQoL) between SDF and other non-surgical treatments for dental caries in children.[20] Duangthip[21] also found that using SDF for caries arrest in preschool children is safe, with no significant adverse effects reported by parents.

Our study supports the effectiveness of SDF in preventing and arresting caries in primary teeth, as reported in previous research [6] and we also found positive patient-centred outcomes. These results emphasise the importance of considering the application type and protocol when using SDF for caries management. Our results suggest that the biannual application of SDF with BM, for dental caries is effective in preventing major complications at the patient level. In contrast, annual application with BM did not show a significant difference from the placebo with BM in terms of major complications. While more research is required to explore the long-term impact of SDF and other non-invasive caries management interventions on PCOs, our study further supports their use in children.

The results of our study, along with the increased interest in non-invasive treatments during the COVID-19 pandemic[22], suggest that the use of Silver Diammine Fluoride (SDF) could be a valuable addition to caries management protocols. The national survey of Latvian dentists[22] showed a general openness to incorporating non-invasive treatments, such as SDF. Nevertheless, there is a need to find the best way to get uptake of these treatments by dentists and these might include better dissemination of information, hands-on training, and reliable evidence to support their use and have them offered to parents. The findings suggest that parents and child patients are receptive to non-invasive options and that they may not be the barrier to their use, as is sometimes assumed by dentists. It is important that options are presented for parents and dentists, together with child patients, can make the best decision for the child, with them at the centre of the treatment planning.

In conclusion, our findings suggest that use of SDF-biannually together with BM effectively prevents PCOs as major and minimal complications and parents and children are highly satisfied with the non-invasive treatments. This clinical trial adds to the growing evidence supporting using non-invasive caries management interventions for children. There was a combined approach to managing the lesions where behaviour change was promoted with the parent in a supportive manner. This is a recommended part of this approach to caries management.[23] The combined use of the medicament and behaviour change makes it difficult to ascertain the individual effect of each on the results. Further research could evaluate the long-term effectiveness of non-invasive treatments and the impact of training on the adoption and effectiveness of non-invasive treatments in clinical practice.

Methods

Ethics and protocol registration

The study protocol was prepared and approved by the Riga Stradins University Ethics Committee (Nr. 6-1/06/20) on 28/05/2020. The research strictly adhered to the guidelines outlined in the Declaration of Helsinki,[24] with the parents or legal guardians of all participants granting their written informed consent. Subsequently, the study commenced, and the protocol in English was published later, on 30/06/2021 in the ISRCTN registry (ISRCTN17005348, https://www.isrctn.com/ISRCTN17005348). The ethics committee amended and approved the protocol to include children with genetic disorders, autism, and heart disease (2-PĒK-4/627/2022). The study recruited participants between September 2020 and May 2021, with follow-up examinations conducted from September 2021 to August 2022. Participants could participate voluntarily and were guaranteed conventional treatment if they declined. It was an additional treatment option during the waiting period for conventional treatment, addressing the limited availability of public services for children in Latvia. The study followed standard emergency intervention protocols from the Institute of Stomatology of Riga Stradins University (IS-RSU). Riva Star SDF and Tiefenfluorid were the two medications used in the study for caries treatment. Both are commercially available and registered for professional use in Latvia. Riva Star SDF contains 35-40% silver fluoride and 15-20% ammonium,[25] while Tiefenfluorid contains 0.4% CuSiF6, 10.9% MgSiF6, 0.1% NaF, and 9.6% Ca(OH)2. [25] This clinical trial is reported according to the CONSORT-Outcomes (for combined completion of CONSORT 2010[26] and CONSORT-Outcomes 2022 items[27] (**Supplementary Table S1)** involved six randomised groups.

- ## Study design and setting

The superiority randomised single-blind clinical trial with six parallel arms was conducted at the IS-RSU Paediatric Department in Riga, Latvia, from 01/09/2020 to 01/08/2022.

Sample size calculation

To achieve a study power of 80% and an alpha error of 0.05, we calculated the sample size for a three-treatment factorial design with two protocols, requiring 49 children for each group to detect a 20% difference[28] in major complication proportions.[29] To account for possible losses during the observation time, 294 children were needed. To ensure sufficient enrollment, we planned to involve 70 children in each group, resulting in 420 children across all groups. Our sample size calculation was based on which caries treatment method would show a lower frequency of complications in managing early childhood caries compared to placebo. The allocation ratio was 1:1

Participant Selection

Parents were invited to participate through social media and during consultations at the IS-RSU. Inclusion criteria: children up to 6 years of age with at least one ICDAS-3 lesion and whose parents provided informed consent. Exclusion criteria: children who had received SDF treatment previously, refusal of masking or randomisation.

Eligible participants were referred to a clinical operator (IM) at the IS-RSU, who provided information on the study, treatment groups, and potential adverse effects. Informed consent was obtained from parents.

Clinical examination

Clinical examination was conducted by a trained and calibrated examiner (IM, Intra-examiner kappa: 0.853 for ICDAS 1 level; non-cavitated enamel lesion level; k=0.872 for activity) who took the child's history and used a pre-existing questionnaire to collect information on health, dietary habits, hygiene practices, and previous dental experiences.The presence or absence of visible plaque was recorded, and carious lesions were assessed using ICDAS[30] codes, with simplified registration of filled surfaces. Lesion activity was assessed according to Nyvad criteria,[31] and complications were registered as PUFA code.[30] Carious lesions were registered at tooth level, choosing the highest score of surface/surfaces. Parents received tailored advice on caries prevention based on the child's needs.

Randomisation: sequence generation, allocation concealment and implementation

The researcher (IM) was responsible for randomisation and allocation concealment. A simple randomisation sequence was generated using coloured cards with a 1:1 allocation ratio. The allocation was performed sequentially, and the sequence was implemented by one researcher (IM). Attempts were made to conceal the researcher's identity, but due to the characteristics of the products, this was not possible, and thus the researcher was aware of the allocation.

Interventions

The intervention was multi-component according to the Medical Research Council definition[32], consisting of two parts:

Component 1) All participants' parents received a behavioural modification (BM) intervention using passive interviewing to collect data whilst raising awareness of the importance of good oral hygiene and dietary practices and use of motivational interviewing principles to help parents to focus on changing one or two habits, emphasising toothpaste containing more than 1000ppm fluoride. The counseling sessions, lasting 45 minutes or more, were provided individually to each child's family.

Component 2) Carious lesions were treated with one of three compounds: placebo (P), Tiefenfluorid (TF) (0.4% CuSiF6 x 6 H2O, 10.9% MgSiF6 x 6 H2O, 0.1% NaF, 9.6% Ca(OH)2) from Humanchemie GmbH, Alfeld (Leine), Germany, or silver diammine fluoride (SDF) (35-40% silver fluoride, 15-20% ammonium) from SDI Riva Star (SDI Bayswater, Victoria, Australia). The SDF was commercially acquired. TF was donated by the company, which had no involvement in the study's design, analysis, or dissemination. We did not receive a certificate of analysis from the manufacturer, nor did we conduct independent verification of the contents.

There were two application regimes for each of the compounds (1) involved four weekly baseline applications, while the biannual protocol (2) entailed applications at six-month intervals.).

This meant six multi-component intervention protocols were as follows:

1. P1: Placebo used with one annual regime (four applications, one week apart) with behavioural modification;
2. P2: Placebo used with single applications twice per year and behavioural modification at both visits;
3. TF1: Tiefenfluoride used with one annual regime (four applications, one week apart) with behavioural modification;
4. TF2: Tiefenfluorid used with single applications twice per year and behavioural modification at both visits;
5. SDF1: SDF used with one annual regime (four applications, one week apart) with behavioural modification;

6. SDF2: SDF used with single applications twice per year and behavioural modification at both visits.

Each child was treated individually, and the interventions were carried out by one of the six paediatric dentists at the clinic, who were trained in advance on the study protocol and the application procedures with all the products used in the study.

Operator and participant blinding

Several measures were taken to blind parents and children to the arm they were allocated:

1. To reduce the impact of taste, we used standardised communication during the application process and informed them in advance about the possibility of a sweet or unusual taste. In cases where taste sensitivity was expected, we used a cotton roll with sweet toothpaste to isolate the lesion and minimise taste perception.
2. All parents were informed about possible delayed black pigmentation from the substance applied and that arrested lesions may become dark over time.

Baseline characteristics

- At baseline, demographic information was collected, and parents provided information about toothbrushing frequency, toothpaste use, and consumption of sweets and sugary drinks. The researcher (IM) conducted a clinical examination to record the presence of visible plaque, d1mft and d3mft indices, and the number of active lesions.

Follow-up examination

Patients who received biannual interventions were recalled at 6 and 12 months, while patients who received annual interventions were recalled for evaluation only 12 months after the intervention. No interim analyses or stopping guidelines were implemented in this study.

Outcomes and outcome measures

Primary Outcome (major complications)

Intervention effectiveness is measured as the absence of major complications. Major complications were defined as dental pain, emergency visits, tooth extraction, or endodontic treatment in the last 12 months. The assessment was through a) questioning the parent about any dental emergencies or complaints over the past year, b) from the patient's records about visits, emergencies, and GA sessions. and c) from clinical examination using the same methodology as in the baseline examination for healthy, filled, carious, and missing teeth and whether there was evidence of pulpal or periodontal pathology using the PUFA code.[30] For our analysis, we measured outcomes on a per-patient basis. Patients with any complications were categorised as cases; those without as successes.

Secondary Outcomes:

1. Minor complications - composite outcome comprising lesion activity measured in Nyvad criteria[31] or lesion progression in the 12-month follow-up defined as a positive change in ICDAS baseline status or any new lesion or ongoing activity/progression of previously treated lesions
2. Satisfaction:
    a. Parent would be happy to have that treatment again for the same child or another of their children (5-point Likert scale);
    b. Parental satisfaction with the aesthetic result (5-point Likert scale); and
    c. Child's satisfaction with the aesthetic result (3-point visual analogue scale).

- By employing these composite variables, we aimed to capture important treatment outcomes for parents and children and ensure that our findings were patient-centred. Any adverse effects reported by parents regarding the impact of the treatment on their children were recorded. No changes were made to the trial outcomes after the trial commenced.

Covariates:

1. Gender (female, male) and age (in months) of the participants.
2. Presence of visible plaque (yes or no). Plaque presence was visually assessed using an examination light, and no probe was utilised prior to ICDAS measurement.
3. Frequency of tooth brushing (twice or more times per day; every evening; in mornings or less than once per day; seldom or never) and how often parents brush their children's teeth (every evening; frequent if more than three times per week; seldom or never).

4. Intervention adherence was evaluated to understand its impact on the outcome better. Adherence was optimal if the participant received all intervention sessions as per the group-according protocol, less frequent if the participant missed at least one planned visit, and more frequent if the participant came to additional visits during the follow-up period.
5. Cooperation was assessed using a modified scale from Venham[33] and categorised as good (Venham's codes 0-1), average (codes 2-3), or low (codes 4-5).
6. Number of active lesions at baseline as a covariate.

These variables were included to control for their potential influence on the outcome and isolate the intervention's effect.

Statistical analysis

The data were analysed on an intention-to-treat basis, with the child as the unit of analysis. Clinical records data were analysed in R version after being entered into a secure online form with pseudonymised patient codes. The analysis population for our study was defined as all participants who received at least one intervention and who had at least one follow-up assessment. Participants who dropped out of the study or who were lost to follow-up were excluded from the analysis population. Data were cleaned and verified against clinical records, and missing or unverifiable data were removed. The outcome analysis population was defined as the intention-to-treat population, whereby all randomised participants were included in the analysis regardless of their adherence to the trial protocol. The pattern of missing data was evaluated using the MCAR from the Naniar R package. An exploratory analysis was performed, generating summary tables and visualisations. Proportion tests were used to compare the incidence of major and minor complications across intervention groups in the clinical trial, allowing for a quantitative assessment of the impact of each intervention and identifying significant differences ($p<0.05$) in their effectiveness. We used a generalised linear regression (GLM) model to examine the association between various formulations/protocols and major complications, minor complications, and patient satisfaction while adjusting for covariates. The patient was the unit of analysis, and we accounted for clustering effects by fitting a random intercept model for each child. No outcome data were excluded from the analysis. Results were reported as odds ratios (OR) with 95% confidence intervals (95%CI) and a p-value as a measure of statistical significance.

Declarations

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Author contributions

Conceptualization: I.M., S.E.U..; Data curation: S.E.U.; Formal analysis: I.M. and S.E.U.; Funding acquisition: I.M.; Investigation: I.M., S.E.U., I.V., A.B., E.S., K.K. and N.I.; Methodology: I.M., S.E.U. and N.I.; Project administration: I.M..; Supervision: A.B., E.S., S.E.U. and N.I.; Validation: K.K.; Visualization: S.E.U.; Writing – original draft: I.M., S.E.U. and N.I.; Writing - review & editing: I.M., S.E.U., I.V., A.B., E.S., K.K. and N.I.

Competing Interests

The authors declare no competing interests.

Data Availability

The datasets generated and/or analysed during the current study are available in the Zenodo repository: https://zenodo.org/record/7677435.

Ethics Declarations

The study protocol was approved by the Riga Stradins University Ethics Committee (Nr. 6-1/06/20). During the study, we updated the protocol, changed inclusion criteria, and obtained new approval from the Ethics Committee before the publication of the results (2-PĒK-4/627/2022). The study obtained written informed consent from parents before enrolling their children. The consent form contained the study's nature, objective, procedures, risks, benefits, and confidentiality measures. The parents were given enough time to review and ask questions before signing the form. Participation was voluntary, and patients could withdraw without prejudice. Informed consent forms are securely stored, with limited access only, with the permission of the principal investigator to ensure confidentiality and ethical compliance. The research strictly adhered to the guidelines outlined in the Declaration of Helsinki. [24]

Clinical trial registration number

ISRCTN registry: ISRCTN17005348, https://doi.org/10.1186/ISRCTN17005348, registration date: 30/06/2021.

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Figures

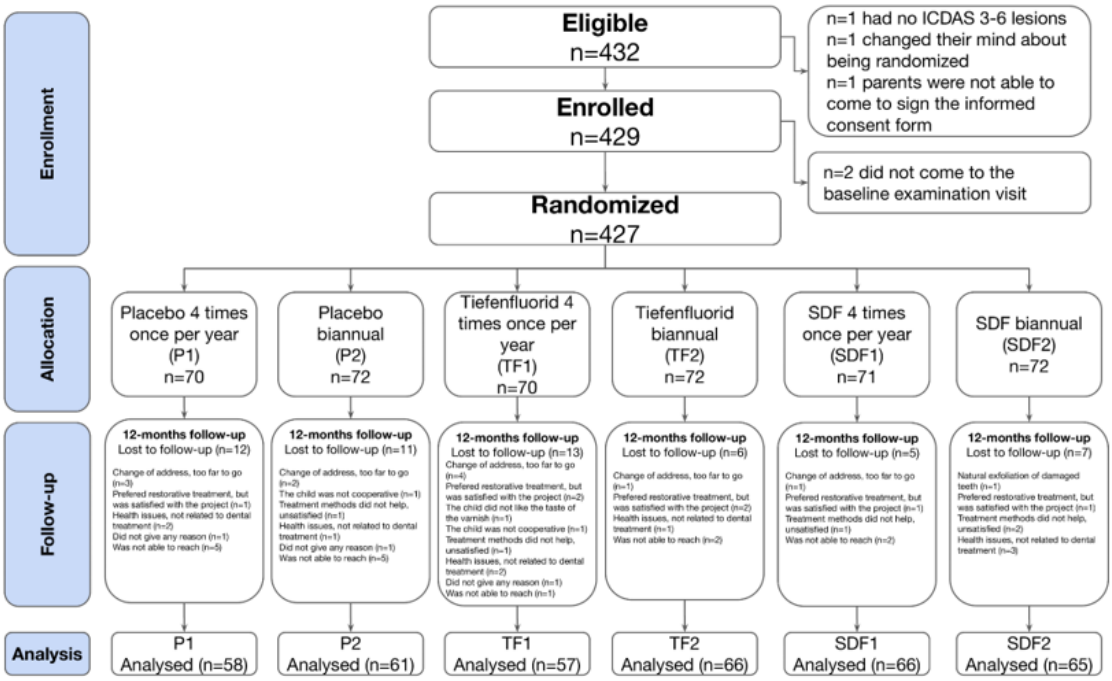

Figure 1

CONSORT Flow diagram illustrating participant enrollment, randomisation, allocation, follow-up, and analysis.

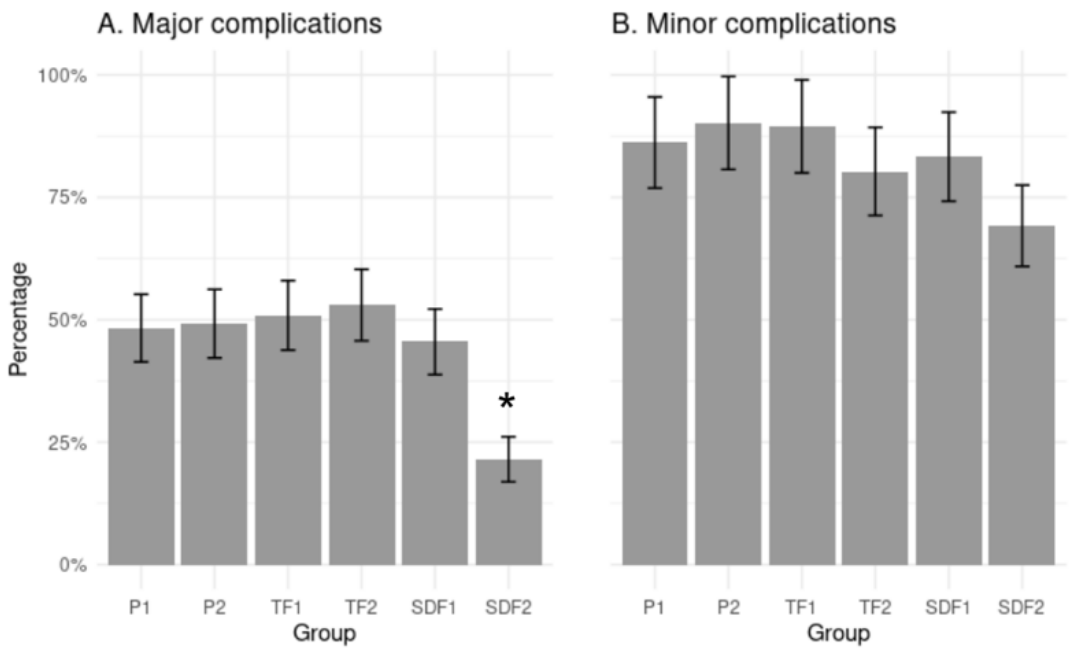

Figure 2

The proportion of (A) major and (B) minor complications by intervention group (percentage and standard deviation, * unadjusted proportions test <0.05).

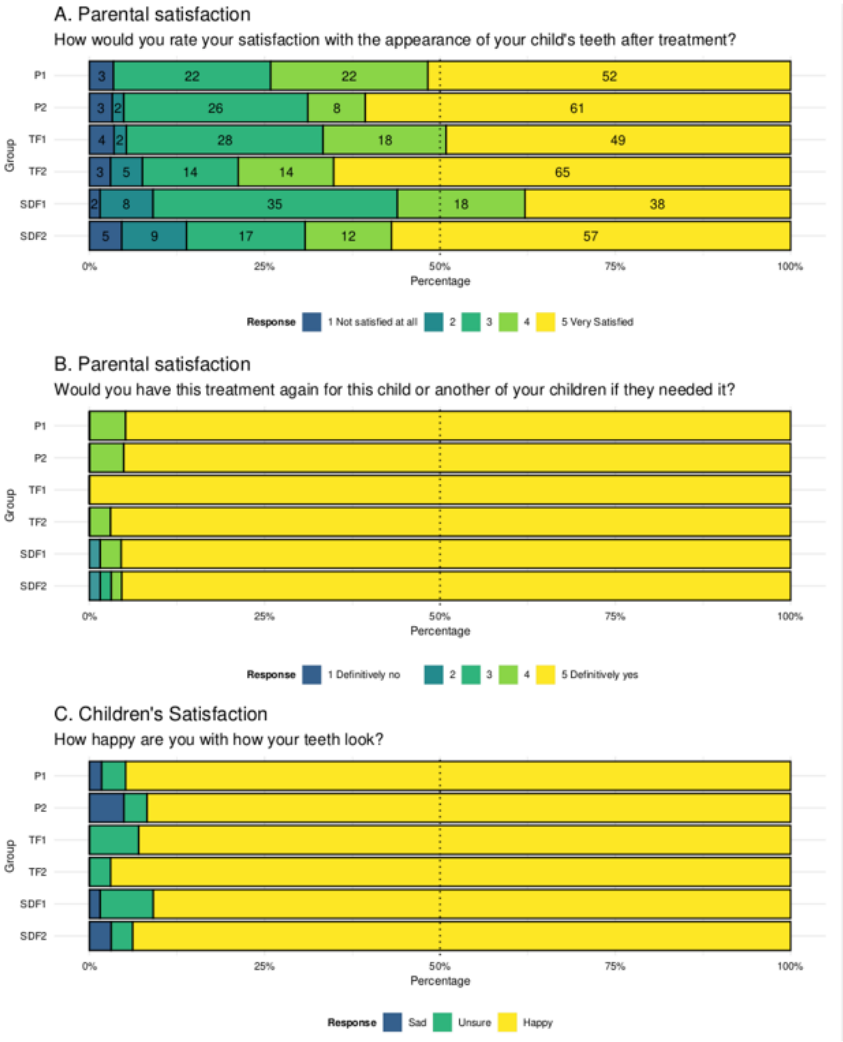

Figure 3

Parental and children's satisfaction with noninvasive caries management methods.

Supplementary Files

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- SupplementaryInformationClinicaleffectivenesschildpatientandparentsatisfactionoftwotopicalfluoridetreatmentsforcariesarandomisedclinicaltrial.pdf