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New non-invasive treatments for the control and treatment of early childhood caries

Submission date
16/06/2021

Recruitment status
No longer recruiting

Registration date
30/06/2021

Overall study status
Completed

Last Edited
08/04/2024

Condition category
Oral Health

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[X] Individual participant data

Plain English summary of protocol

Background and study aims
Oral health is essential to general health and significantly influences the development of children. Dental caries (tooth decay) has a high economic and social impact due both to the treatment costs as well as the days lost in school by children and at work by their parents, and the effects that remain throughout life. Also, as caries are associated with high sugar intake, they are a predictor of risk for heart disease and diabetes in children and adults. The causes of early childhood caries are complex and the main associated factors are high sugar consumption and inadequate oral hygiene. The traditional operative treatment of cavities often fails, especially when tooth restoration is performed at an early age. Less invasive caries treatment strategies have been proposed that would have the advantage of lowering the costs of care as well as decreasing the number of tooth extractions. Fluoride applications are effective at decreasing the incidence of early childhood caries while silver diamine fluoride (SDF) is effective at arresting the progression of cavities. However, a usual adverse effect of SDF is that it stains the teeth black. New formulations have appeared that replace silver with copper (Tiefenfluorid) to avoid this. At this moment, the effectiveness of Tiefenfluorid in permanent teeth is proven, but there are no studies in deciduous dentition (milk teeth), or clinical studies comparing the effectiveness of these non-invasive treatments. Also, there is a gap in knowledge about which treatments are most effective and how the interval between applications influences clinical effectiveness. To date, it is known that a biannual application is better than one application per year, but other application schedules have not been studied. This study could provide important information on the effectiveness, cost-effectiveness and potential side-effects of these methods for patients. The main of the study is to find out which high-concentration fluoride application method and schedule is more effective at preventing complications arising from early childhood caries in preschool children.

Who can participate?
Children aged 1-6 years with severe early childhood caries

What does the study involve?
Participants are randomly allocated into six groups - three treatment methods (silver diamine fluoride [SDF], fluoride solution with copper ions (Tiefenfluorid) and placebo [without any active substance, but ensuring nonrestorative caries control]), applied at two different intervals: 1)

semiannual and 2) four times weekly. Parents (direct caregivers) will be advised about tooth cleaning and diet and are recommended to brush their teeth with toothpaste that contains fluoride. The researchers will record general information about the child, hygiene and dietary habits, plaque, and caries damage and activity at the beginning of the study and 12 months later. The researchers will measure pain and inflammation history, the number of extracted and restored teeth during the observation period (12 months), the change of the activity of the carious lesions, the parents' and children' satisfaction with the treatment and with the way teeth look, the direct costs of the treatment and any undesirable side effects.

What are the possible benefits and risks of participating?
All participants will receive an immediate benefit - individualized recommendations, which will be given using motivational interviewing principles, assuring that everybody has the chance to change their behaviour and avoid cavities in the future. One-third of participants will receive up to date the most effective non-restorative cavity control method with silver diamine fluoride, the others will benefit from toothbrushing with fluoride and other interventions, including Tiefenfluoride, the effectiveness of which is not clear at the moment. All participants will have access to immediate care in case of progression and complications, including attention in general anaesthesia for free. There are no registered allergic reactions to the used materials, but the researchers will avoid including children who have experienced several allergic reactions. They will also never use an amount close to the maximum dose of the products to avoid any health effects.

Where is the study run from?
Riga Stradins University (Latvia)

When is the study starting and how long is it expected to run for?
March 2020 to February 2023

Who is funding the study?
1. Riga Stradins University (Latvia)
2. European Regional Development Fund (European Union)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003400-41

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
BZ01A1

Study information

Scientific Title
Treatment of early childhood caries with three different topical fluoride treatments: a randomised clinical trial

Acronym
NoCaries

Study objectives
Application of topical fluoride treatment methods will lower the complication rate of early childhood caries from 30% to 10% in preschool children.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 28/05/2020, Riga Stradins University Research Ethics Committee (Dzirciema Street 16, Riga, LV-1007, Latvia; +371 (0)67061596; pek@rsu.lv), ref: Nr.6-1/06/20

2. approved 23/12/2022, Amendment approved by Riga Stradins University Research Ethics Committee (Dzirciema Street 16, Riga, LV-1007, Latvia; +371 (0)67061596; pek@rsu.lv), ref: 2-PĒK-4/627/2022

Study design
Randomized triple-blinded placebo-controlled single-centre clinical trial with six parallel groups

Primary study design
Interventional

Study type(s)
Treatment, Efficacy

Health condition(s) or problem(s) studied
Early childhood caries

Interventions
Patients are allocated into groups using restricted randomization - there are pre-numbered six colour cards; patients are allocated to the group which corresponds to the number of the next card after signing informed consent.

The first placebo group: placebo application twice with a 6-month interval and a recommendation to brush teeth with a toothpaste containing fluoride (F content of at least 1000 ppm)
The second placebo group: placebo application four times with a week's interval and a recommendation to brush teeth with a toothpaste containing fluoride (F content of at least 1000 ppm)
The first SDF group: Riva Star SDF (35-40% silver fluoride, 15-20% ammonium) application twice with a 6-month interval and a recommendation to brush teeth with a toothpaste containing fluoride (F content of at least 1000 ppm)
The second SDF group: Riva Star SDF application four times with a week's interval and a recommendation to brush teeth with a toothpaste containing fluoride (F content of at least 1000 ppm)
The first Tiefenfluorid group: Tiefenfluorid (0.4% $CuSiF_6 \times 6\ H_2O$, 10.9% $MgSiF_6 \times 6\ H_2O$, 0,1% NaF, 9.6% $Ca(OH)_2$) application twice with a 6-month interval and a recommendation to brush teeth with a toothpaste containing fluoride (F content of at least 1000 ppm)
The second Tiefenfluorid group: Tiefenfluorid application four times with a week's interval and a recommendation to brush teeth with a toothpaste containing fluoride (F content of at least 1000 ppm)

For ethical reasons, a negative control group will not be used – in each of the study's groups, the parents (direct caregivers) will be given advice about tooth cleaning and diet, observing motivational intervention principles and recommending brushing teeth with toothpaste that contains fluoride, which is defined as non-restorative caries treatment and which has also proven its effectiveness in stopping caries damage.

Intervention Type
Behavioural

Primary outcome(s)
1. Pain history during the observation period, assessed as Yes/No by two calibrated dentists at the 12 months follow-up visit
2. Abscess history during the observation period, assessed as Yes/No by two calibrated dentists at the 12 months follow-up visit
3. The number of newly extracted or otherwise surgically treated teeth during the observation period, assessed using medical records at the 12 months follow-up visit

Key secondary outcome(s))
1. The change in the overall activity of caries as Active/Non-active, assessed by two calibrated dentists at the 12 months follow-up visit
2. The progression and change of activity of every lesion, assessed by International Caries Detection and Assessment System (ICDAS) (progression) and Nyvad (activity) criteria, at the 12 months follow-up visit
3. The parent's satisfaction with the way their children's teeth look, assessed by a questionnaire asking: "Are you satisfied with the way your child's teeth look?" and "Would you agree to repeat the treatment procedure used?" on a 5-point Likert scale, at the 12 months follow-up visit

4. The child’s satisfaction with their teeth, measured by the visual analogue scale (VAS) with three points (happy, not sure, sad) at the 12 months follow-up visit
5. The child’s feelings during the treatment, measured by the modified Wong-Baker scale with three options (no hurt, hurts a little, hurts a lot), during every appointment (depending on treatment group can be assessed at baseline, 1, 2, 3 weeks and 12 months; or at baseline, 6 and 12 months)
6. The direct costs of the treatment and the cost-effectiveness, calculated as EUR spent per treatment protocol; EUR per prevented major complications (patient-level - pain, abscess, extraction) and EUR per prevented minor complications (tooth-level - progression of caries lesion), calculated at the 12 months follow-up visit
7. The treatment method’s undesirable side effects, assessed by parent questionnaire at the 12 months follow-up visit

Completion date
28/02/2023

Eligibility

Key inclusion criteria
1. Children aged 1-6 years
2. Have at least one active caries damage with cavitates (comply with the diagnosis of severe early childhood caries [S-EEC])
3. Wish to participate in the study
4. Parents agree to participate in the study and sign a consent form

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
1 years

Upper age limit
6 years

Sex
All

Total final enrolment
420

Key exclusion criteria
1. The child arrives with an adult who doesn’t have the right to sign a consent form, and the person responsible for the child cannot be present
2. Chronic or serious acute general illness

3. In the last month has used medications that could affect the secretion of saliva
4. Previously received treatment with products that have a high level of fluoride concentration

Date of first enrolment
01/09/2020

Date of final enrolment
31/05/2021

Locations

Countries of recruitment
Latvia

Study participating centre
Riga Stradins University
Institute of Stomatology
Dzirciema Street 20
Riga
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Sponsor information

Organisation
Riga Stradiņš University

ROR
https://ror.org/03nadks56

Funder(s)

Funder type
University/education

Funder Name
Rīgas Stradiņa Universitāte

Alternative Name(s)
Rīga Stradiņš University, Rīga Stradiņš University, Universitas Rigensis Stradina, Riga Medical Institute, Medical Academy of Latvia, RSU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Latvia

Funder Name
European Regional Development Fund

Alternative Name(s)
Fondo Europeo de Desarrollo Regional, Europäischer Fonds für regionale Entwicklung, Европейски фонд за регионално развитие, Evropský fond pro regionální rozvoj, Fundo Europeu de Desenvolvimento Regional, ERDF, FEDER, EFRE, ΕΦΡΡ, EFRR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing plan as of 24/10/2023:
The datasets generated and analysed during the current study are available in the Zenodo repository: https://zenodo.org/record/7677435.

Previous IPD sharing plan:
The original data, along with the codebook and analysis scripts, will be published in the RSU institutional data repository at https://dataverse.rsu.lv/.
The data will consist of csv sheets with the data of the patients and R analysis scripts. The dataset will be called dataset and the dataset generated by the research, including also preprints and technical reports, will be called dataverse.
The dataverse corresponding to this investigation will receive a digital object identifier (DOI).
The citation has seven components. Five are human-readable: the author(s), title, year, data repository (or distributor), and version number. Two components are machine-readable: the DOI and the universal numeric fingerprint (UNF).
The data generated will be de-identified using R's randomizeR package, removing all personal information.
The naming convention for the archives will be date in yyyymmdd-version-identifier.extension format.
The use of spaces will be avoided, being replaced by -.
The WHO classification will be used, so the metadata associated with this classification, available

at https://www.who.int/publications/data/gho/indicator-metadata-registry/imr-details/3812, will be used.
The original anonymized data will be published with restricted access once the data cleaning and exploratory analysis stage is completed. The data will be made public at the time of sending the final report to a peer-reviewed journal, with its DOI corresponding to the data associated with the research.
The data will be embargoed until the final report is accepted, at which time it will become publicly available. No access restrictions will be applied to the data once the final project report has been accepted.
The formats to be used will be csv for spreadsheet data, R Markdown for analysis scripts, pdf and csv for codebooks and odt or txt for text files. If any other format is used, the alternative open version will be used.
The versions of the programs used for data analysis will be included.

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/04/2024	08/04/2024	Yes	No
Dataset	Data and the research script	25/02/2023	24/10/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file			08/07/2021	No	No
Protocol file	version 2.0	25/08/2021	27/02/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes