

Forskningsamverkan – KOF-syd

Projektbeskrivning/information

Projektets titel

Bacterial acid tolerance – A new target for fluoridated milk in caries prevention.

Sammanfattning

The aim of the project is to investigate whether caries is caused by specific disease-inducing activities in dental biofilms and if caries can be prevented by interfering with the development of aciduric phenotypes using fluoride in milk. We have so far recruited 88 adolescents (12-years-old in 2012) who are currently participating in the clinical trial: 41 subjects at the Public Dental Health Clinic in Alvesta and 47 subjects at the Public Dental Health Clinic in Sölvesborg. Thus 88 participants are presently drinking milk supplemented with fluoride/control solution on a daily basis. Therefore we consider the project to be well on track with the protocol.

Caries risk assessment performed at the Clinics shows that 15 % of the participants had previous caries experience (high caries risk) in Alvesta and 34% in Sölvesborg. Therefore, we judge the caries prevalence to be sufficiently high to enable us to see the effect of the fluoride intervention.

Plaque samples for determination of acid tolerance from the 88 participants have been analysed. There has been enough material in all samples to be able to determine the acid tolerance of the bacteria. In Alvesta 71% of the participants had plaque acid tolerance score values of 1 or 2 indicating a low acid tolerance. For Sölvesborg the same figure was 51%.

Medverkande

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Medel från externa bidragsgivare (VR, STF osv)

Från	År	Summa
Borrows Foundation	2012	2,4 miljoner
KOF-Syd	2012	Ca 20% tjänst varje klinik

Projektets mål

We will test whether caries is caused by specific disease-inducing activities in dental biofilms and can be treated by interfering with the development of aciduric phenotypes. The novelty of this idea is that acid tolerance is presented as a target for fluoride treatment. The following research questions are addressed:

- Does fluoride in milk (0.75-1.0mg in 200ml), administrated daily, inhibit the development of acid tolerance in plaque biofilms?
- Does fluoride in milk (0.75-1.0mg in 200ml), administrated daily, prevent caries?
- Can low caries progression be correlated to a low level of acid tolerance in plaque biofilms and vice versa?

Projektets betydelse

Caries is one of the most common biofilm-mediated diseases worldwide. Although not life-threatening, it is associated with high costs for society [WHO-report 2006 (1)]. In developing countries where socioeconomic and cultural factors support consumption of high levels of fermentable carbohydrates, 60-90% of schoolchildren have caries and even in Western populations it is a serious problem for 5-10% of adults. In Sweden, the previously observed decline in caries incidence has ceased (2) and almost one third of 26-year olds have more than six decayed or filled approximal tooth surfaces (3). In the near future, the numbers of individuals in caries-susceptible groups, such as the elderly where the potential for self-care is limited and for those on medication, are expected to increase steadily. Thus, as stated in the SBU-report on caries (2007), novel approaches to prevention and treatment are needed. Therefore in this proposal, we will focus upon how fluoride affects bacterial physiology in dental plaque and our hypothesis is that fluoride can contribute to the prevention of caries through inhibition of the development of acid-tolerant phenotypes (4).

Projektbeskrivning

Study Settings and Participants. This is a randomized controlled trial that will take place in general dental clinics within the Public Dental Health Service in four counties in Southern Sweden (Halland, Blekinge, Kronoberg and Kalmar). Participants eligible for the trial are schoolchildren aged 12-13 years. The inclusion criterion is the presence of at least one permanent first molar in approximal contact with a permanent first or second premolar.

A power of 80% requires the random selection of 140 patients in both the treatment and the control groups to reveal a 15% difference between the two groups, giving a total of 180 patients. This is based on a population where 25% of the children in the control group and 10% of those in the intervention group would be expected to develop a new caries lesion during the three-year study period. These calculations are based on data on caries incidence from the clinics participating in Oral Public Health Care in Sweden. At each clinic, 45 patients will be included in each group resulting in a total of 360 individuals. This will allow a drop out of 80 patients (22%). Patients assessed as having risk for caries, as determined by acid tolerance in plaque and clinical risk assessment, will be distributed randomly to the control and intervention group. This will ensure that patients with risk for caries are present in both the control and intervention groups.

Intervention. In addition to their normal oral hygiene routines, patients in the intervention group will drink low doses of fluoride (5mg/L NaF) in 100 ml of cow's milk on a daily basis. Patients in the control group will consume 100 ml of the same milk with the same volume of sterile water as for fluoride. The fluoride/placebo solution will be supplied as individually packaged daily doses (0.5 g fluoride/L in 1 ml sterile water). In contacting the guardian of the patient, we will ask about the daily routine milk consumption of the patient. We expect the routine consumption of milk, at least in the evening, to be very common and cover 95% of the patients. The consumption of milk will be regulated with the participants instructed to drink the milk in one session in the early evening.

Compliance. The patients live in small towns and have a high degree of social anchorage. School and dental clinic are within walking distance and the patients have generally attended these clinics for oral health care since the age of three. In order to ensure regular contact with the participants we will administer two months of fluoride/placebo solution on each visit to the clinic. At the same time as the patients collect the solutions they will be rewarded with a voucher that is valid at a local sport shop. Also, the patient will be given a ticket for a lottery at the end of a one-year period. The prize will be one iPad per year, one for each clinic comprising 90 children. Travel costs will be covered.

A dental nurse or dental hygienist at each clinic will be responsible for monitoring the compliance and all dental health professionals will be active in ensuring that the adolescents fulfil their commitments. When the patient is scheduled for refilling of fluoride solutions, an interview will be held by the clinician locally in charge of communication with the participants to discuss compliance problems. If needed, a contact will also be established with the guardian of the patient.

Implementering av projektet

The research questions addressed in this project originate from clinical needs in oral health care. The hypothesis that caries can be prevented and treated by interfering with the development of aciduric *phenotypes* has been studied in *in vitro* models and the promising results of these studies are now to be translated into clinical research in different settings. To enhance the commitment and knowledge among the staff at the clinics, working groups of experts and caregivers will be formed and the theory underpinning the project, methodology and expected outcomes will be communicated to them. In addition to this knowledge exchange within these specific clinics, the clinical practice community in general as well as the scientific and educational communities will be informed via oral and written presentations in international and national fora and peer-reviewed journals. To support the implementation of the results obtained in our studies in oral health care, recommendations and guidelines, including other relevant results of clinical research, will be formulated.

Tidplan

2012-2017

Preliminära resultat

FIRST INTERIM REPORT (IR1)

Project: Bacterial acid tolerance – A new target for fluoridated milk in caries prevention, project number 028/MUS

Location of project: Oral biology, Faculty of Odontology, Malmö University, Malmö, Sweden

Duration of project: 4 years

Date of commencement: November 2012

Period covered by the report: Aug 2012 – Febr 2013

Authors of report:

Professor Gunnel Svensäter

Professor Julia Davies

Researcher Jessica Neilands

Professor Björn Axtelius

Personnel involved:

Malmö University - Professor Gunnel Svensäter, Professor Julia Davies, Professor Björn Axtelius, Professor Madeleine Rohlin, Researcher Jessica Neilands, Technician Ulrika Troedsson

Dental Clinic in Alvesta, Sweden - Dentist Christina Stebring, Dental

hygienist Maria Hilding and dental nurses

Dental Clinic in Sölvesborg, Sweden - Dentist Carina Norberg, Dental hygienist Ingela Franzén and dental nurses

Date of submission of report: 2013-03-08

SUMMARY:

The aim of the project is to investigate whether caries is caused by specific disease-inducing activities in dental biofilms and if caries can be prevented by interfering with the development of aciduric phenotypes using fluoride in milk. We have so far recruited 88 adolescents (12-years-old in 2012) who are currently participating in the clinical trial: 41 subjects at the Public Dental Health Clinic in Alvesta and 47 subjects at the Public Dental Health Clinic in Sölvesborg. Thus 88 participants are presently drinking milk supplemented with fluoride/control solution on a daily basis. Therefore we consider the project to be well on track with the protocol.

Caries risk assessment performed at the Clinics shows that 15 % of the participants had previous caries experience (high caries risk) in Alvesta and 34% in Sölvesborg. Therefore, we judge the caries prevalence to be sufficiently high to enable us to see the effect of the fluoride intervention.

Plaque samples for determination of acid tolerance from the 88 participants have been analysed. There has been enough material in all samples to be able to determine the acid tolerance of the bacteria. In Alvesta 71% of the participants had plaque acid tolerance score values of 1 or 2 indicating a low acid tolerance. For Sölvesborg the same figure was 51%.

Aims and Objectives

We will test whether caries is caused by specific disease-inducing activities in dental biofilms and can be treated by interfering with the development of aciduric phenotypes. The novelty of this idea is that acid tolerance is presented as a target for fluoride treatment. The following research questions are addressed:

- Does fluoride in milk (0.75-1.0mg in 200ml), administrated daily, inhibit the development of acid tolerance in plaque biofilms?
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- Can low caries progression be correlated to a low level of acid tolerance in plaque biofilms and vice versa?

Progress Measured against Protocol

Achievements:

- We have applied for, and been granted, ethical approval enabling the project to be undertaken (2012-09-06 - Regional Ethical Board in Lund, Sweden; Dnr 2012/294).
- We have established a functioning research group comprised of academic staff at Malmö University and clinicians at four different dental clinics in southern Sweden. We consider a close relationship is crucial for the success and completion of this project. We have had meetings on a regular basis as well as one major calibration meeting.
- With aid of a pilot study we have established
 - a reliable procedure for the collection and transport to laboratory of plaque samples.
 - a protocol for assessment of compliance
 - routines for the distribution of fluoride and placebo solutions
- The X-ray equipment at the clinics currently running has been calibrated in order to ensure the quality of the radiographs. The following baseline measurements have been made:
 - -clinical examinations including bite wing X-ray
 - -risk assessments performed by clinician
 - -determination of acid tolerance in plaque samples.
- The patients have been assigned to intervention and control groups.
- We have recruited the following participants (12-years-old in 2012) who are currently participating in the clinical trial: 41 subjects at the Public Dental Health Clinic in Alvesta and 47 subjects at the Public Dental Health Clinic in Sölvesborg.
- Thus 88 participants are currently drinking milk supplemented with fluoride/control solution on a daily basis. Therefore we consider the project to be well on track with the protocol.

Details of results and findings

Recruitment figures at the two clinics currently running

	Clinic in Alvesta	Clinic in Sölvesborg
Total invited to participate	92	72
Number who declined	36	7
Agreed but appointment cancelled due to illness (to be recalled at a later date)	5	8
Inclusion criteria not fulfilled* (to be recalled	10	10

at a later date)		
Initially agreed but dropped-out after starting to rinse	0	4
Actively participating in study	41	47

* primary teeth remaining/permanent teeth not fully erupted

Risk assessment at baseline

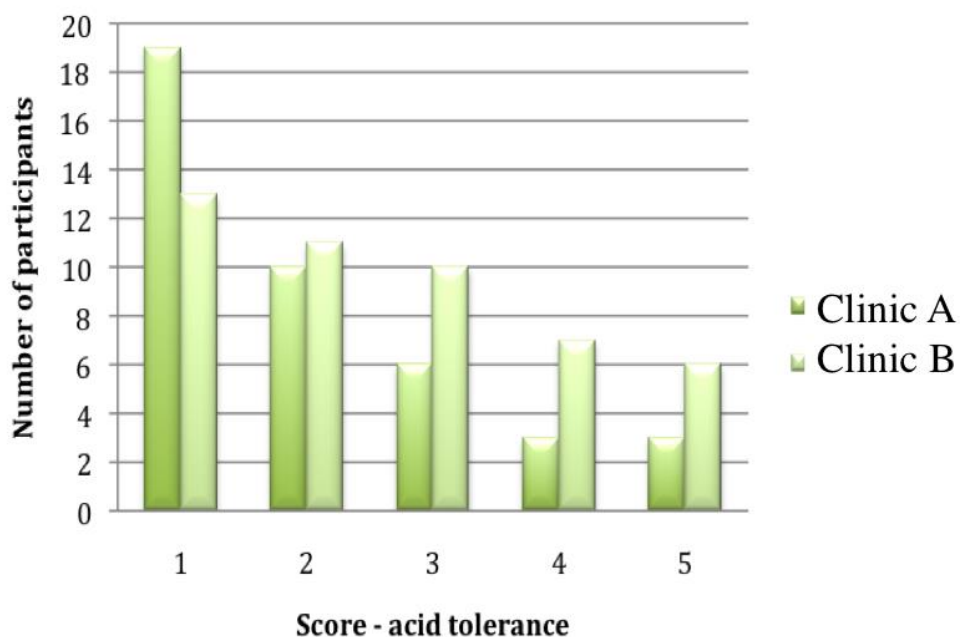
This was performed by clinicians at the baseline examination. The assessment is based on previous caries experience according to ICDAS (visual/tactile caries lesion on buccal/palatinal surfaces), or dentin caries/progressive enamel caries over the previous two years.

Risk Assessment	Total	Clinic #1	Clinic #2
High caries risk	22	6	16
Low caries risk	66	35	31

Fifteen % of the participants had previous caries experience (high caries risk) in Alvesta and 34% in Sölvesborg. Therefore, we judge the caries prevalence to be sufficiently high to enable us to see the effect of the intervention.

Determination of acid tolerance in plaque samples

Plaque samples for determination of acid tolerance have been taken from



Financial

Financial support received for Nov 2012 – April 2013: 28 643€

EXPENSES related to the project	
Stationary/stamps for the clinics	437 €
Plaque Sampling (Quick sticks, transport tubes)	671 €
Gift vouchers for participants	1865 €
Start-up kit for participants (glasses for milk, tubes and holders for intervention solutions, fluoride solutions, sterile water)	7529 €
Consumables for laboratory (BacLight, Ibidi flow cells, pipettes, chemicals)	2590 €
Travel (academic staff transport to clinics)	724 €
Project Meetings (calibration meeting, academic and clinical staff together)	5967 €
Total	19783 €

Future plans

Completion of recruitment at clinics in Alvesta and Sölvesborg
Initiation of recruitment at Clinics in Färjestaden and Tvååker
6-month follow-ups at clinics in Alvesta and Sölvesborg.

Staff

No changes in staff involved in the project.

Publications

An article presenting the project in The journal of the Swedish Dental Association, November 2012 (Tandläkartidningen).

Referenser

- (1) WHO-report. Oral health: action plan for promotion and integrated disease prevention. Executive board 120th session, provisional agenda item 4.6. EB120/10, 2006.
- (2) National Board of Health and Welfare. Report on caries prevalence in children and adolescent from 1985 to 2005. (In Swedish).
- (3) Mejäre I, Stenlund H, Zelezny-Holmlund C. Caries incidence and lesion progression from adolescence to young adulthood: a prospective 15-yearcohort study in Sweden. Caries Res 2004; 38:130- 41.

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- (7) Sansone C, Van Houte J, Joshipura K, Kent R, Margolis HC. The association of mutans streptococci and non-mutans streptococci capable of acidogenesis at a low pH with dental caries on enamel and root surfaces. *J Dent Res* 1993;72:508-16.
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