Arginine and Caries Prevention: A Systematic Review

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Key Words
Arginine · Arginine-fluoride toothpaste · Caries · Caries prevention · Dental care

Abstract
Objectives: To evaluate the available evidence that the use of arginine-containing dental care products prevents the development of new caries lesions and the progression of existing lesions. Search Methods: We performed a systematic literature search of databases including PubMed, the Cochrane Library and EMBASE. Selection Criteria: We selected randomized controlled trials of treatment with arginine in fluoride-containing dental products measuring dental caries incidence or progression in children, adults and elderly subjects. Data Collection and Analysis: Two review authors independently assessed trials for risk of bias and evaluated overall study quality using the GRADE classification. Main Results: Due to conflicts of interest and weak transferability to Swedish conditions, no conclusions can be drawn from studies on the effects of arginine-fluoride toothpaste in children. Arginine-containing toothpaste costs about 40% more than basic fluoride toothpaste; to determine whether it is more cost-effective, the higher cost must be considered in relation to any additional caries-preventive effect. The literature review also disclosed some questionable research ethics: in several of the studies, the children in the control group used non-fluoride toothpaste. Toothpaste without fluoride is not as effective against dental caries as the standard treatment – fluoride toothpaste – which has a well-documented effect. This contravenes the fundamental principles of research ethics. Conclusion: At present there is insufficient evidence in support of a caries-preventive effect for the inclusion of arginine in toothpastes. More rigorous studies, and studies which are less dependent on commercial interests, are required.

Caries Research

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ar intake, acid production decreases and the pH rises again.

Caries prevention encompasses measures used to prevent initial dissolution of the dental enamel (primary caries prevention) and also to arrest the progression of early lesions (areas of demineralized enamel) which have not yet deteriorated to cavitation (secondary caries prevention). The same measures are usually applied for both primary and secondary prevention.

The widespread use of fluoride toothpaste has contributed to a dramatic reduction in caries incidence worldwide: daily brushing with fluoride toothpaste is acknowledged as the most cost-effective method of preventing caries. With application of fluoride, the dissolution of the hydroxyapatite crystals can be effected.

Arginine has recently been introduced as an additive to toothpaste and other fluoride-containing dental care products. Initially marketed for the treatment of sensitivity of exposed necks of teeth, arginine is now being promoted as a caries-preventive agent. Arginine is an amino acid that occurs naturally in a range of food products and in the saliva. It is metabolized by arginolytic bacteria which produce ammonia-like substances [Wijeyeweera and Kleinberg, 1989], which leads to an increase in the pH in the oral biofilm [Huang et al., 2012]. This thereby counteracts the acidic environment conducive to the growth of acid-resistant bacteria.

The purpose of this literature review is to evaluate the evidence supporting the caries-preventive effect of the addition of arginine to dental care products, with special reference to preventing the development of new caries lesions and the progression of existing caries lesions, in children and adults.

Materials and Methods

Inclusion Criteria

The following questions were addressed:

- What is the preventive effect, measured as caries incidence (DMFT/DMFS), of arginine in fluoride toothpaste, fluoride rinses or other fluoride-containing dental products?
- What is the preventive effect, measured as caries progression, of arginine in fluoride toothpaste, fluoride rinses or other fluoride-containing dental products?

In accordance with the PICO model (participants, interventions, control, outcome):

Participants

- Children (primary dentition): high and low caries risk
- Children and adolescents (permanent dentition): high and low caries risk
- Adults: high and low caries risk
- Elderly subjects (≥75 years): high and low caries risk

Interventions

- Arginine in toothpaste, mouthwash, or other fluoride-containing dental products

Control

- Toothpaste, mouthwash, or other fluoride-containing dental products

Outcome Measures

- Dental caries incidence (primary prevention) in the primary dentition, measured as dft/dfs (or individual components of either index separately):
  - Primary outcome measure: by clinical examination, diagnostic imaging or by other means, e.g. electrical conductance measurements (ECM), fibre-optic transillumination (FOTI), or equivalent diagnostic method
  - Secondary outcome measures: by quantitative light-induced fluorescence (QLF)
- Dental caries incidence (primary prevention) in the permanent dentition, measured by DMFT/DMFS (or individual components of either index separately):
  - Primary outcome measure: by clinical examination, diagnostic imaging or by other means, e.g. ECM, FOTI, or equivalent diagnostic method
  - Secondary outcome measures: by QLF
- Caries progression (secondary prevention) in individual permanent teeth:
  - Primary end point: measured by clinical, diagnostic imaging or by other means, e.g. ECM, FOTI, or equivalent diagnostic method
  - Secondary end points: measured by QLF

Types of Studies

- Randomized controlled trials (including in situ studies)

Duration of Treatment

- Clinical diagnosis, imaging diagnosis, or other diagnostic method (ECM, FOTI) ≥2 years (≥6 months for high-risk groups)
- QLF ≥2 months (≥2 months for high-risk groups)

Exclusion Criteria

Studies with ‘split-mouth’ design.

Literature Search Strategy

The most recent literature search was conducted during April 2014 (Cochrane Library, February 2014). Four databases were searched: PubMed, the Cochrane Library, Centre for Reviews and Dissemination (CRD) and EMBASE. There were no language restrictions. For a more detailed description of the search terms and limitations used, see table 1.

Figure 1, a flow chart, presents the number of abstracts retrieved, included and excluded articles and the stage of exclusion. Abstracts identified according to the inclusion criteria were screened independently by two review authors. If at least one reviewer considered an abstract to be relevant, it was included and its full text was read.
Table 1. Search strategies

<table>
<thead>
<tr>
<th>Search terms</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PubMed via NLM – April 9, 2014</strong></td>
<td></td>
</tr>
<tr>
<td>Dental caries</td>
<td></td>
</tr>
<tr>
<td>3 1 OR 2</td>
<td>60,472</td>
</tr>
<tr>
<td><strong>Dentifrices</strong></td>
<td></td>
</tr>
<tr>
<td>6 4 OR 5</td>
<td>25,817</td>
</tr>
<tr>
<td>7 3 OR 6</td>
<td>75,348</td>
</tr>
<tr>
<td><strong>Arginine</strong></td>
<td></td>
</tr>
<tr>
<td>10 8 OR 9</td>
<td>98,412</td>
</tr>
<tr>
<td><strong>Combined sets</strong></td>
<td></td>
</tr>
<tr>
<td>11 7 AND 10</td>
<td>339</td>
</tr>
<tr>
<td><strong>Cochrane Library via Wiley – February 24, 2014</strong></td>
<td></td>
</tr>
<tr>
<td>Dental caries</td>
<td></td>
</tr>
<tr>
<td>MeSH descriptor: [dental caries] explode all trees OR MeSH descriptor: [dental plaque] explode all trees</td>
<td>3,838</td>
</tr>
<tr>
<td>OR MeSH descriptor: [dentifrices] explode all trees</td>
<td></td>
</tr>
<tr>
<td>Caries or plaque or dentifrice* or tooth-paste* or toothpaste*t.i.ab.kw (word variations have been searched)</td>
<td>10,509</td>
</tr>
<tr>
<td>Fluoride varnish* or topical fluoride* or fluoride gel* or fluoride tablet* or fluoride supplement* or fluoride drop* or fluoride rins* or fluoridation*</td>
<td></td>
</tr>
<tr>
<td>1 OR 2</td>
<td>10,533</td>
</tr>
<tr>
<td><strong>Arginine</strong></td>
<td></td>
</tr>
<tr>
<td>MeSH descriptor: [arginine] explode all trees</td>
<td>1,147</td>
</tr>
<tr>
<td>Arginin*:t.i.ab.kw (word variations have been searched)</td>
<td>2,732</td>
</tr>
<tr>
<td>4 OR 5</td>
<td></td>
</tr>
<tr>
<td><strong>Combined sets</strong></td>
<td></td>
</tr>
<tr>
<td>3 AND 6 = 52</td>
<td></td>
</tr>
<tr>
<td><strong>Embase via Elsevier – April 9, 2014</strong></td>
<td></td>
</tr>
<tr>
<td>Dental caries</td>
<td></td>
</tr>
<tr>
<td>‘Dental caries’/exp/mj OR ‘tooth plaque’/exp</td>
<td>9,673</td>
</tr>
<tr>
<td>Caries*:ab,ti OR carious:ab,ti OR ‘tooth plaque’:ab,ti OR ‘dental plaque’:ab,ti OR (tooth NEXT/1</td>
<td>9,062</td>
</tr>
<tr>
<td>(hypominerali* OR deminerali* OR reminerali*):ab,ti)</td>
<td></td>
</tr>
<tr>
<td>1 OR 2</td>
<td>13,285</td>
</tr>
<tr>
<td><strong>Dentifrices</strong></td>
<td></td>
</tr>
<tr>
<td>'Toothpaste'/exp/mj OR ‘anticaries agent’/exp/mj OR ‘mouthwash’/exp OR ‘fluoride varnish’/exp OR</td>
<td>2,371</td>
</tr>
<tr>
<td>'dental floss’/exp</td>
<td></td>
</tr>
</tbody>
</table>
Data Extraction and Quality Assessment

Two of the review authors independently undertook an assessment of relevance and quality, as well as data extraction from included studies. Any differences were resolved by consensus discussion. When necessary, a third review author was consulted. The quality of the included studies was assessed using a protocol for the assessment of randomized studies. The scientific quality of the evidence in the primary studies was graded according to GRADE, as strong, moderate, limited or insufficient [Guyatt et al., 2008, 2011]. After the evidence has been summarized, GRADE provides explicit criteria for rating the quality of evidence that include study design, risk of bias, imprecision, inconsistency, indirectness and publication bias. When summarizing the evidence from randomized controlled studies, as in this systematic review, the preliminary quality of the evidence is the highest possible – strong (++++).

A conservative approach was used: if a feature was not reported, it was assumed to be absent. If the answer to a particular question was unclear, it was discussed by the group, and a decision was reached as to whether the study should be classified as having a low, moderate or high risk of bias.

To assess clinical heterogeneity, the primary studies were scrutinized with respect to study population, intervention and outcomes. Statistical heterogeneity was estimated using $\chi^2$ (Q-value) and $I^2$ analyses. A $p$ value of <0.05 ($\chi^2$) and an $I^2$ value of >50% were...
interpreted as significant heterogeneity. A meta-analysis was undertaken using the random effect model. Mean differences were calculated using Review Manager 5.3, Copenhagen, the Nordic Cochrane Centre, the Cochrane Collaboration, 2014.

Contact with the Authors
The authors of all the studies which form the basis of the evidence-graded results were contacted regarding their participation in the studies [Kraivaphan et al., 2013; Srisilapanan et al., 2013; Yin et al., 2013a, b]. The Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) received information about the degree of involvement of all authors of the included studies (preparation of manuscripts, QLF images, analysis of QLF images and statistical analysis).

Results

Literature Search
Seven studies met the inclusion criteria, and the risk of bias was assessed. In 5 of the studies, the subjects were children [Acevedo et al., 2005; Kraivaphan et al., 2013; Srisilapanan et al., 2013; Yin et al., 2013a, b]. The subjects of the other 2 were adults [Hu et al., 2013; Souza et al., 2013a]. As these 2 studies were both considered to be at high risk of bias, further analysis of treatment effects on adults could not proceed. Of the 5 studies on children, 1 was at high risk of bias and 4 were at moderate risk. The evidence-graded results are based on the 4 studies at moderate risk, 3 of which measured caries progression with QLF, while the fourth study measured caries incidence in terms of DMFT/DMFS (table 2). The main difference between the studies on adults and those on children was that the techniques measuring the outcomes in the adult studies were not validated and were at higher risk of bias. A summary of excluded studies and studies at high risk of bias is presented in table 3.

In all 4 studies with a moderate risk of bias, the intervention comprised the use of fluoride toothpaste (1,450 parts per million, ppm) with the addition of arginine (1.5%). Fluoride toothpaste (1,450 ppm) served as the control (table 2).

Table 2. Characteristics and quality assessment of included studies

<table>
<thead>
<tr>
<th>Study, country</th>
<th>Population</th>
<th>Study period</th>
<th>Intervention</th>
<th>Control</th>
<th>Risk of bias, comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yin et al., 2013a, China</td>
<td>n = 298, age: 10–12 years</td>
<td>6 months</td>
<td>Dentifrice with 1.5% arginine + 1,450 ppm fluoride (MFP) in a calcium base (at least twice daily)</td>
<td>Dentifrice with 1,450 ppm fluoride (MFP) in a calcium base (at least twice daily)</td>
<td>– Moderate risk of bias – Unclear randomization process – No published study protocol – Conflict of interest – Second control group (dentifrice without fluoride) was not assessed in this review (152 subjects)</td>
</tr>
<tr>
<td>Srisilapanan et al., 2013, Thailand</td>
<td>n = 341, age: 7–13 years</td>
<td>6 months</td>
<td>Dentifrice with 1.5% arginine + 1,450 ppm fluoride (MFP) and an insoluble calcium compound (at least twice daily)</td>
<td>Dentifrice with 1,450 ppm fluoride (MFP) and an insoluble calcium compound (at least twice daily)</td>
<td>– Moderate risk of bias – Somewhat unclear randomization process – No published study protocol – Conflict of interest</td>
</tr>
<tr>
<td>Yin et al., 2013b, China</td>
<td>n = 308, age: 9–13 years</td>
<td>6 months</td>
<td>Dentifrice with 1.5% arginine + 1,450 ppm fluoride (MFP) and an insoluble calcium compound (at least twice daily)</td>
<td>Dentifrice with 1,450 ppm fluoride (NaF) in a silica base (at least twice daily)</td>
<td>– Moderate risk of bias – Unclear randomization process – No published study protocol – Conflict of interest – Second control group (dentifrice without fluoride) was not assessed in this review – Dentifrice in intervention and control differed in other aspects apart from arginine</td>
</tr>
<tr>
<td>Kraivaphan et al., 2013, Thailand</td>
<td>n = 6,000, age: 6–12 years</td>
<td>2 years</td>
<td>– I1: dentifrice with 1.5% arginine + 1,450 ppm fluoride (MFP) and dicalcium phosphate (twice daily) – I2: dentifrice with 1.5% arginine + 1,450 ppm fluoride (MFP) and calcium carbonate (twice daily)</td>
<td>Dentifrice with 1,450 ppm fluoride (NaF) in a silica base (twice daily)</td>
<td>– Moderate risk of bias – Somewhat unclear randomization process – No published study protocol – Conflict of interest – Dentifrice in intervention and control differed in other aspects apart from arginine</td>
</tr>
</tbody>
</table>

MFP = Sodium monofluorophosphate; n = study participants; NaF = sodium fluoride.
Caries Incidence

Evidence-Graded Results

- The quality of the evidence is very low: only 1 included study investigated whether the addition of arginine to fluoride toothpaste had any effect on caries prevention in children, measured as caries incidence (DMFT/DMFS) (+OOO).

- There are no included studies, and thus there is no evidence available on whether the addition of arginine to fluoride-containing dental care products other than fluoride toothpaste has any caries-preventive effect in children, measured as caries incidence (DMFT/DMFS) (+OOO).
There are no included studies, and thus there is no
evidence available on whether the addition of arginine
to fluoride toothpaste has any caries-preventive effect
in adults, measured as caries incidence (DMFT/DMFS).

The results of the single included study investigating
caries incidence are presented in Table 4 [Kraivaphan et al., 2013]. The study was considered to be of moderate
risk of bias (table 5). Published in 2013, it was conducted
in Thailand and had a 2-year follow-up. The children in
the intervention group, using toothpaste with fluoride
and arginine, had a smaller increase in DMFT and DMFS
than those in the control group using fluoride toothpaste.
The mean difference in the increase in DMFT between
the intervention and the control groups was 0.13, and
0.11 teeth. For DMFS the corresponding difference for
both comparisons was 0.15 tooth surfaces. If these results
are correct, the numbers needed to treat would be about
8–10 patients for 2 years to save 1 tooth; to save 1 tooth
surface, the numbers needed to treat would be about 7
patients for 2 years.

As only 1 study has been included (table 6), the quality of the evidence according to GRADE is very low [SBU,
2014].

Caries Progression
Evidence-Graded Results

- For assessing whether the addition of arginine to fluo-
ride toothpaste has any caries-preventive effect in chil-
dren, measured as caries progression, the quality of the
evidence is very low: based on 3 included studies, with
both risk of bias and indirectness (+OOO).
- There are no included studies, and thus there is no
available evidence on whether the addition of arginine
to fluoride-containing dental care products other than
fluoride toothpaste has any effect on caries prevention
in children, measured as caries progression (+OOO).
- There are no included studies, and thus there is no
available evidence on whether the addition of arginine
added to fluoride dentifrices has any effect on caries
prevention in adults, measured as caries progression
(+OOO).

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection bias</th>
<th>Performance bias</th>
<th>Detection bias</th>
<th>Attrition bias</th>
<th>Reporting bias</th>
<th>Conflict of interest</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yin et al., 2013a</td>
<td>high</td>
<td>moderate</td>
<td>moderate</td>
<td>low</td>
<td>high</td>
<td>high</td>
<td>moderate</td>
</tr>
<tr>
<td>Srisilapanan et al., 2010</td>
<td>high</td>
<td>moderate</td>
<td>moderate</td>
<td>low</td>
<td>high</td>
<td>high</td>
<td>moderate</td>
</tr>
<tr>
<td>Yin et al., 2013b</td>
<td>high</td>
<td>moderate</td>
<td>moderate</td>
<td>moderate</td>
<td>high</td>
<td>high</td>
<td>moderate</td>
</tr>
<tr>
<td>Kraivaphan et al., 2013</td>
<td>high</td>
<td>moderate</td>
<td>moderate</td>
<td>moderate</td>
<td>high</td>
<td>high</td>
<td>moderate</td>
</tr>
</tbody>
</table>

Low = Low risk of bias; moderate = moderate risk of bias; high = high risk of bias.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study design</th>
<th>Mean difference</th>
<th>Quality of evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caries incidence measured as DMFT</td>
<td>RCT; 5,096 participants, 1 study [Kraivaphan et al., 2013]</td>
<td>Intervention 1: –0.13 teeth, p = 0.001 Intervention 2: –0.11 teeth, p = 0.007</td>
<td>+OOO</td>
<td>Only 1 study</td>
</tr>
<tr>
<td>Caries incidence measured as DMFS</td>
<td>RCT; 5,096 participants, 1 study [Kraivaphan et al., 2013]</td>
<td>Intervention 1: –0.15 surfaces, p = 0.009 Intervention 2: –0.15 surfaces, p = 0.002</td>
<td>+OOO</td>
<td>Only 1 study</td>
</tr>
</tbody>
</table>

DMFT/DMFS = Decayed, missed and filled teeth/decayed, missed and filled surfaces (permanent teeth); RCT = randomized controlled trials. + out of a possible ++++ in the GRADE score.

- There are no included studies, and thus there is no
evidence available on whether the addition of arginine
to fluoride toothpaste has any caries-preventive effect
in adults, measured as caries incidence (DMFT/DMFS) (+OOO).

As only 1 study has been included (table 6), the quality of the evidence according to GRADE is very low [SBU, 2014].

Caries Progression
Evidence-Graded Results

- For assessing whether the addition of arginine to fluo-
ride toothpaste has any caries-preventive effect in chil-
dren, measured as caries progression, the quality of the
evidence is very low: based on 3 included studies, with
both risk of bias and indirectness (+OOO).
- There are no included studies, and thus there is no
available evidence on whether the addition of arginine
to fluoride-containing dental care products other than
fluoride toothpaste has any effect on caries prevention
in children, measured as caries progression (+OOO).
- There are no included studies, and thus there is no
available evidence on whether the addition of arginine
added to fluoride dentifrices has any effect on caries
prevention in adults, measured as caries progression
(+OOO).
The results on caries progression are summarized in table 7. The 3 studies were considered to have a moderate risk of bias (table 5). All the studies had 6-month follow-ups and were published in 2013. Two studies were conducted in China [Yin et al., 2013a, b] and 1 in Thailand [Srisilapanan et al., 2013]. A meta-analysis of the results shows that the intervention had a positive effect: compared with the control group, the lesions in the intervention group exhibited a greater reduction in the difference in fluorescence between the caries and the surrounding tooth structure (mean difference –4.67, 95% CI –6.34 to –3.01; fig. 2). This means that greater remineralization has occurred in the intervention group.

The quality of the evidence according to GRADE is very low. One point has been deducted because of risk of bias in the included studies, and 2 points for indirectness (table 8). None of the studies had a prepublished trial protocol, and in the included studies randomization was inadequately described. The representatives of the Colgate-Palmolive Company were involved in all steps of the

![Fig. 2. Meta-analysis of caries progression assessed with QLF. IV = Instrumental variable; CI = confidence interval.](image-url)
study leading to a deduction of 1 point for risk of bias (table 8). Caries progression was monitored by QLF, which measures only the change in fluorescence of the enamel (secondary outcome). Finally, the study population is not generalizable to the Swedish population considering factors such as caries prevalence [Norderyd et al., 2015], and taken together this has resulted in the deduction of 2 points for indirectness.

Complications and Side Effects

Evidence-Graded Results

- These outcomes were not investigated in any of the included studies. Thus, there is no evidence as to whether arginine added to fluoride-containing dentifrices causes any complication and/or side effects (+OOO).

Ethics

Consideration of ethical aspects was based on a framework for systematic identification of ethical aspects of health care technologies [Heintz et al., 2015]. The treatment in question does not have an adequate basis on which to determine whether there are any further oral health benefits from daily use compared with conventional procedures in use today. It is therefore not feasible to undertake an ethical evaluation in relation to the treatment effect. The main ethical issues identified in preparing this report have instead been associated with the included studies and research in the field in question. In several of the studies one control substance was non-fluoride toothpaste; thus, the children in this group received treatment which offers poorer protection against caries than the standard method, fluoride toothpaste, which has been shown to be effective. The inclusion of such a control group violates the basic principles of ethics in research. The major objection is that it is unethical with respect to the study participants, but there is also another ethical issue to be addressed: considerable research resources have been allocated to study a question which does not need to be answered. It may be claimed that this is misdirected funding, which thus becomes unavailable for research into other scientific questions which remain unclear. All the studies included in the evaluation originated from and were financed by the company which manufactures the test product. Representatives of the company have also participated in every stage of the studies, raising grave concerns about the issue of impartiality and conflict of interest. Not only are more rigorous studies required, but also studies which are independent of financial interests.

Health Economic Aspects

A systematic review of health economic studies of arginine supplements in dental care products identified 5 studies, but none met the inclusion criteria of the current review. Arginine-fluoride toothpaste costs about 40% more than conventional fluoride toothpaste (www.badrumshyllan.se, December 4, 2014). To determine whether this is cost-effective or not, the extra cost needs to be assessed in relation to the potential additional benefits. As dental care is generally financed by the individual, the relevant question of cost-effectiveness of arginine supplements in dental care products is a matter for the individual. If however, oral hygiene products were to be subsidized from public funds, then it would be necessary to analyse the willingness of society to pay, and the cost-effectiveness. There is no evidence that arginine-fluoride toothpaste is more effective in preventing dental caries than conventional fluoride toothpastes. Thus, as the cost is higher, arginine-fluoride toothpaste cannot be deemed cost-effective at a societal level.

Identified Knowledge Gaps

As no answers to the questions addressed were forthcoming, several scientific knowledge gaps were disclosed.
in the course of this project. This means that there is an inadequate scientific basis on which to determine:
• the preventive effect, expressed as caries incidence (DMFT/DMFS, dmft/dmfs)
• the preventive effect, expressed as caries progression, and
• side effects of arginine in fluoride toothpaste, fluoride rinses or other fluoride-containing dental care products.

Discussion

This systematic overview, undertaken to evaluate the effect of arginine in preventing and arresting caries, has disclosed an inadequate scientific basis for evaluation of the effect of arginine in any of the circumstances in question. There is currently no reason to recommend arginine-fluoride toothpaste in preference to conventional fluoride toothpaste. Revision of this standpoint would have to be based on evidence from independent, more rigorous studies which are not flawed by the shortcomings noted in the course of this review. For example, to varying degrees the randomization process was only briefly presented and not described in detail in the included studies. Other serious shortcomings were that no prepublished trial protocol was available for any of the included studies and that representatives of the company which manufactures the test product, i.e. with clear conflict of interest, participated in every stage of the studies. Several studies were also deemed to be of low quality because of poorly validated methods for classifying and diagnosing caries. The results of the studies with respect to caries progression also comprise an inadequate scientific basis. Poor study quality resulted in deduction of points on the GRADE scale, and 2 points were deducted for poor transferability. The use of QLF to measure the effect on caries progression is also questionable: QLF measures only changes in fluorescence related to the mineral content of the enamel (a secondary measure) and thus reduces transferability. In addition, the study population is not generalizable to Swedish conditions. It became clear that in several of the included studies a positive effect was found in the control groups using non-fluoride toothpaste.

Conclusion

This literature search identified a number of studies which investigated the caries-preventive effects of arginine-fluoride toothpaste in children. However, due to conflicts of interest and weak transferability to Swedish conditions, no conclusions can be drawn from these studies.

Disclosure Statement

In accordance with SBU’s regulations, the experts and scrutineers involved in the project have submitted declarations of conflict of interest. These documents are available at SBU’s head office. SBU has deemed that the declarations confirm that the participants fulfil the requirements of objectivity and impartiality.

Author Contributions

Álfheiður Ástvaldsdóttir: assessment of relevance and quality, manuscript preparation.
Aron Naimi-Akbar: assessment of relevance and quality, meta-analysis, manuscript preparation.
Thomas Davidson: health economic analysis, manuscript preparation.
Agnetta Brolund: literature search, manuscript preparation.
Laura Lintamo: language revision, manuscript preparation.
Anna Attergren Granath: manuscript preparation.
Pernilla Östlund: assessment of relevance and quality, manuscript preparation.

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