Systematic review of studies comparing the anti-caries efficacy of children's toothpaste containing 600 ppm of fluoride or less with high fluoride toothpastes of 1,000 ppm or above

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CRD summary
The review found that 250-ppm fluoride toothpastes were not as effective as 1,000-ppm fluoride toothpastes at preventing dental caries in the permanent dentition. Data comparing 500-ppm and 1,000-ppm fluoride toothpastes were limited and further research is required. This was a good-quality systematic review and the authors' conclusions are likely to be reliable.

Authors' objectives
To compare the effectiveness of low and high fluoride toothpastes in preventing dental caries.

Searching
MEDLINE, EMBASE, Dissertation Abstracts, SERFILE 2000 and the Cochrane Controlled Trials Register were searched from inception to January 2001; the search terms were reported. The authors also checked the reference lists of all eligible trials and handsearched eight dentistry journals (from January to May 2001). Only trials reported in the English language were included in the review.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. The duration of the trials ranged from 24 to 36 months.

Specific interventions included in the review
Studies that compared toothpastes containing 600 ppm fluoride or below with those containing 1,000 ppm fluoride or above were eligible for inclusion. The studies evaluated fluoride in the form of sodium fluoride (NaF) and/or monofluorophosphate (MFP). Five trials reported water fluoridation levels, which were below 0.2 ppm. Two trials used 0.2% NaF mouthwash every 14 days as an additional source of fluoride during the trial period.

Participants included in the review
Participants of any age were eligible for inclusion. The included studies consisted of both boys and girls aged between 2 and 13 years.

Outcomes assessed in the review
The authors did not state any inclusion criteria relating to outcomes. However, they reported that the following outcomes were recorded where available: the mean difference in caries increment measured as dmft/DMFT; the mean difference in caries increment measured as dmfs/DMFS; and the mean difference in caries increment measured as DFS/DFT. The authors did not give further details of these outcomes, which appeared to be standard epidemiological indices for measuring caries status. The systems used for the diagnosis of caries were bitewing radiographs and visual examination. The diagnostic threshold varied between the studies.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The Jadad scale was used to assess the quality of the included studies. This validated scale assesses randomisation, blinding and the description of withdrawals. Two reviewers independently assessed the validity of the included studies.
and any disagreements were resolved by consensus. Only studies that scored at least 3 out of a possible 5 were included in the review. The level of inter-rater agreement was assessed using the weighted kappa statistic.

Data extraction
Two reviewers independently extracted data from the included studies directly into a pre-designed data extraction table. Data were extracted on the following: fluoride formula and concentration, type of abrasive, duration, year and location of the study, number and age of participants, brushing manner, diagnostic criteria and thresholds used, description of reversals, water fluoridation levels, and the outcome measures. Data from studies of toothpastes with a fluoride concentration below 600 ppm were split into two subgroups: those containing 250 ppm fluoride or less and those containing 500 to 600 ppm fluoride. Weighted mean differences (WMDs) of DFS and DFT were calculated, along with their 95% confidence interval (CI).

Methods of synthesis

How were the studies combined?
The overall WMD and 95% CI were calculated using a fixed-effect model. Publication bias was assessed using funnel plots. The authors also attempted to assess the presence of language bias by searching MEDLINE using the same keywords, but not limiting the search to the English language: they stated that none of the studies identified compared low and high fluoride toothpastes, therefore any bias would have been minimal.

How were differences between studies investigated?
The authors stated that statistical heterogeneity was assessed, but did not state the method used. A sensitivity analysis was used to assess the effects of different outcome measures.

Results of the review
Seven RCTs with 5,570 participants were included in the review.

Inter-rater agreement on the assessment of study validity was 0.864 (weighted kappa). One of the included studies achieved a score of 3 on the Jadad scale, two achieved a score of 4 and four achieved a score of 5. The funnel plot indicated that publication bias was unlikely.

Two studies could not be included in the meta-analysis as they failed to report the baseline levels of caries, or the standard error or standard deviation. Therefore, the remaining 5 studies were combined in a meta-analysis. Since only one study assessed 500-ppm fluoride toothpastes, comparisons were only made between 250-ppm and 1,000-ppm fluoride toothpastes; this was assessed in all 5 trials that were eligible for inclusion in the meta-analysis.

There were statistically significant decreases in DFS increment in the 1,000-ppm toothpaste group compared with the 250-ppm toothpaste group in studies where MFP was the control paste (n=2; P=0.002) and NaF was the control paste (n=3; P=0.0005), with overall WMDs of 0.60 (95% CI: 0.22, 0.99) and 0.70 (95% CI: 0.3, 1.09), respectively. Heterogeneity was not statistically significant in either of these analyses.

Statistically significant decreases in DFT increment in the 1,000-ppm toothpaste group compared with the 250-ppm toothpaste group were also obtained: in studies where MFP was the control paste (n=2, P=0.004) the overall WMD was 0.33 (95% CI: 0.10, 0.56), and in studies where NaF was the control paste (n=3, P=0.0009) the overall WMD was 0.38 (95% CI: 0.16, 0.61). Whilst heterogeneity was not statistically significant in the analysis of MFP as the control paste, heterogeneity was of borderline statistical significance in the analysis of NaF as the control paste (P=0.048).

In a sensitivity analysis that excluded the 2 studies in which 0.2% NaF mouthwash was used every 14 days, the difference between the 250-ppm and 1,000-ppm fluoride groups was still statistically significant (P=0.002) in favour of the 1,000-ppm toothpaste, with an overall WMD in DFS increment of 0.66.

Authors' conclusions
Toothpastes containing 250 ppm fluoride were not as effective as those containing 1,000 ppm fluoride at preventing...
dental caries in permanent dentition. The authors stated that data comparing 500-ppm with 1,000-ppm fluoride toothpastes were very limited and further research is required.

**CRD commentary**

The review question was clear in terms of the study designs, participants and interventions of interest. The authors did not state explicit inclusion criteria relating to the outcomes of interest. Several relevant electronic databases were searched, with search terms reported, and this was supplemented with scanning of reference lists and dentistry journals. However, no attempt to seek unpublished studies was made and only English language studies were included in the review; the possibility of publication bias and language bias cannot, therefore, be ruled out. The authors attempted to assess the presence of publication bias but, owing to the small number of studies, this might not have been reliable. The authors also attempted to assess the presence of language bias.

The quality of the included studies was assessed using a validated scale, applied independently by two reviewers, and their level of agreement was assessed. The data extraction was also performed by two independent reviewers. However, the authors did not state how the studies were assessed for relevance to the review, thus the potential for reviewer error or bias could not be assessed for this process. The authors provided adequate details of the included studies. The methods used to combine the studies seemed appropriate and the authors assessed statistical heterogeneity.

Although publication bias and language bias could not be ruled out, on the whole this was a good-quality systematic review and attempts were made to reduce various sources of bias. Therefore, the authors' conclusions are likely to be reliable.

**Implications of the review for practice and research**

Practice: The authors stated that their review only looked at the effectiveness of low fluoride toothpastes at preventing caries and did not assess fluorosis, which must be taken into consideration when recommending a fluoride concentration for toothpaste. However, they stated that they believe 250 ppm should not be recommended in areas where fluoride levels in water are low, owing to its low anti-caries efficacy.

Research: The authors suggested that future trials should be appropriately powered double-blind RCTs that follow the guidelines set out in the Consolidated Standards of Reporting Trials (CONSORT) statement. The trials should present baseline data, and the diagnostic criteria used should be more accurate and able to detect caries at an early stage if possible. A further suggestion was that such trials should ideally compare toothpastes containing 500 ppm and 1,000 ppm fluoride in children younger than 3 years old to assess the anti-caries difference on primary teeth, and that these studies should include a follow-up examination to assess differences in fluorosis between the groups. The authors also suggested that it may be possible to consider combining low fluoride toothpastes with other non-fluoride agents, such as xylitol, to increase their anti-caries efficacy.

**Bibliographic details**

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