Fluoride supplements, dental caries and fluorosis: a systematic review

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CRD summary
The review found weak and inconsistent evidence that fluoride supplements prevented dental caries in primary teeth and strong evidence of benefit for permanent teeth. Mild to moderate fluorosis was a significant side effect. The review was limited by language bias, unclear inclusion criteria, inadequate reporting of study characteristics and poor-quality primary studies. The authors’ conclusions require caution.

Authors’ objectives
To determine whether fluoride supplementation in children aged up to 16 years prevented dental caries and whether it increased the risk of dental fluorosis.

Searching
For effectiveness studies, MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), EBM Reviews and EMBASE were searched from inception to June 2006. Search terms were available from the authors. Reference lists of included studies and of a previous review and the proceedings of two workshops (1990 and 1994) were checked. For fluorosis studies, the reviewers updated the search strategy of a previous review in which MEDLINE was searched from inception, experts in the field were consulted and search terms were reported (see Other Publications of Related Interest). Both searches were restricted to studies in English.

Study selection
Randomised controlled trials (RCTs) of fluoride supplementation to prevent dental caries in children aged up to 16 years were eligible for inclusion as effectiveness studies. Studies were required to compare a group that received fluoride tablets, lozenges or drops (with or without use of fluoride toothpaste) versus controls not exposed to any source of systemic fluoride (water, salt or milk). Studies that reported data suitable for meta-analysis on the independent contribution of fluoride supplements in children to their risk of fluorosis were eligible for inclusion as fluorosis studies.

Most participants in the included effectiveness studies were younger than five years old (range prenatal to 16 years). About half of the studies used fluoride regimens similar to those recommended by the American Dental Association (ADA). Interventions included fluoride tablets, drops, lozenges, mouthwash and/or varnish, with or without vitamins. Control interventions included placebo, vitamins or alternative types of fluoride supplementation (toothpaste, fluoridated water). Outcomes were measured with various scoring tools for decayed, missing or filled surfaces of primary and/or permanent teeth. Duration of follow-up ranged from two to 11.5 years (where reported).

In the fluorosis studies, participant ages ranged from six months to 14 years. Outcomes were prevalence of fluorosis and fluorosis severity score with a variety of scoring tools. Only fluorosis studies published since a previous systematic review (see Other Publications of Related Interest) were reported in detail in the current review.

More than one reviewer selected the studies. Disagreements were resolved by consensus.

Assessment of study quality
Aspects of study validity assessed for effectiveness studies were: blinding; randomisation method; training and reliability of outcome assessors; participant withdrawal rate; and reasons for withdrawal. Studies were rated according to their risk of bias: low (all validity criteria met), moderate (randomisation method reported and withdrawal rate under 30%) or high (other studies). More than one reviewer independently conducted the assessment.

Data extraction
Mean between- or within-group changes in outcome scores, p values, risk ratios, odds ratios, 95% confidence intervals and/or attributable risk percentages were extracted from individual studies and reported in tables.

More than one reviewer extracted the data. Disagreements were resolved by consensus.
Methods of synthesis
Studies were combined in a narrative synthesis grouped into effectiveness and fluorosis studies. Effectiveness studies were subdivided by fluoride regimen (in line with ADA recommendations or not) and by participant age.

Results of the review
Seventeen studies were included in the review. Twelve were effectiveness studies (sample numbers not reported). Risk of bias was high (high bias) in seven of these and moderate (moderate bias) in five. Seven studies were described as randomised. Nine studies were single or double blinned. Seven studies had withdrawal rates of 30% or more (range 5% to 81%). The other five studies were cross-sectional or case-control fluorosis studies (n=5,294).

Effectiveness: Among studies that used ADA-recommended doses of fluoride, two (both high bias) reported significant benefit from the intervention among children younger than six years and a third (moderate bias) reported no statistically significant difference between the groups. All four studies that used ADA-recommended doses of fluoride among children aged six to 16 years (two moderate bias, two high bias) reported significant benefit from the intervention (p<0.5 to p<0.001). Effects were stronger for teeth erupting during the study (one study, high bias). Among five studies of other fluoride doses, three (two high bias, one moderate bias) reported a benefit from the intervention in at least one study group. The other two (one high bias, one moderate bias) reported no statistically significant difference between the groups.

Fluorosis: All five relevant studies confirmed a statistically significant association between the intervention and mild-to-moderate fluorosis.

Authors’ conclusions
There was weak and inconsistent evidence that fluoride supplements prevented dental caries in primary teeth and strong evidence of benefit for permanent teeth. Mild to moderate fluorosis was a significant side effect.

CRD commentary
The objectives of the review were clear and relevant sources were searched for studies. Exclusion of two non-English studies meant that the review was prone to language bias. The inclusion criteria for effectiveness studies were not adhered to, as the review included at least one non-randomised study and in two studies controls were apparently exposed to fluoride. The inclusion criteria for fluorosis studies were not clearly explained. Important details about of the included studies were not systematically reported (such as sample size and study design). It appeared that steps were taken to minimise risks of reviewer bias and error by having more than one reviewer undertake the processes of study selection, validity assessment (of effectiveness studies) and data extraction. It appeared that the validity of fluorosis studies was not assessed. The decision to combine the studies by narrative synthesis appeared appropriate given the heterogeneity between them. The quality of the studies was taken into account in interpreting the findings.

This review was limited by language bias, unclear inclusion criteria, inadequate reporting of study characteristics and poor-quality primary studies. The authors’ conclusions require caution.

Implications of the review for practice and research
Practice: The authors stated that use of fluoride supplements in the first six years of life (especially the first three years) was associated with a significant increase in fluorosis. Current guidelines on use of fluoride supplements in this age group should be reviewed.

Research: The authors stated that research was required into the social impact of fluorosis and to assess the trade-off between the aesthetic impact of fluorosis and risk of dental caries.

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