

Using a fluoridated supplement with a high fluoride concentration in children aged under 6 years may increase the risk of fluorosis

Abstracted from

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Topical fluoride as a cause of dental fluorosis in children. *Cochrane Database Syst Rev* 2010; issue 1

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Question: In children using topical fluorides what is the risk of developing fluorosis?

Data sources The Cochrane Oral Health Group's Trials Register, Cochrane Central Register of Controlled Trials, Medline, Embase, BIOSIS, Dissertation Abstracts and LILACS/BBO databases were searched. Also, reference lists from relevant articles and five journals (Community Dentistry and Oral Epidemiology, Caries Research, Journal of Dental Research, British Dental Journal, Journal of Public Health Dentistry) were searched by hand, and experts in the field of preventive dentistry and oral epidemiology contacted.

Study selection Studies [randomised controlled trials (RCT), quasi-RCT, cohort studies, case-control studies and cross-sectional surveys] were selected if they had included children under the age of 6 years when topical fluorides were administered, and in which fluoride toothpastes, mouthrinses, gels, foams, paint-on solutions and varnishes were compared with an alternative fluoride treatment, placebo or no intervention group.

Data extraction and synthesis Data from all selected studies were extracted by two review authors. Risk ratios (RR) for controlled, prospective studies and odds ratios (OR) for case-control studies or cross-sectional surveys were extracted or calculated. Where both adjusted and unadjusted risk ratios or OR were presented, the adjusted value was included in the meta-analysis.

Results From 3573 identified papers, 25 studies were included: two RCT, one cohort study, six case-control studies and 16 cross-sectional surveys. Only one RCT was judged to be at low risk of bias. The other RCT and all observational studies were judged to be at moderate to high risk of bias. Studies were included in four intervention/ exposure comparisons. A statistically significant reduction in fluorosis was found if brushing of a child's teeth with fluoride toothpaste commenced after the age of 12 months [OR, 0.70; random-effects 95% confidence interval (CI) for topical fluoride, 0.57–0.88; data from observational studies]. Inconsistent but statistically significant associations were found between occurrence of fluorosis and starting use of fluoride toothpaste/toothbrushing before or after the age of 24 months (data from observational studies). From the RCT, use of higher concentrations of

fluoride was associated with an increased risk of fluorosis. No significant association between the frequency of toothbrushing or the amount of fluoride toothpaste used and fluorosis was found.

Conclusions There should be a balanced consideration of the benefits of topical fluorides in caries prevention and the risk of the development of fluorosis. Most of the available evidence focuses on mild fluorosis. There is weak unreliable evidence that starting the use of fluoride toothpaste in children aged <12 months may be associated with an increased risk of fluorosis. The evidence if use begins between the age of 12 and 24 months is equivocal. If the risk of fluorosis is of concern, the fluoride level of toothpaste for young children (under 6 years of age) is recommended to be lower than 1000 parts per million (ppm). More evidence from studies with low risk of bias is needed. Future trials assessing the effectiveness of different types of topical fluorides (including toothpastes, gels, varnishes and mouthrinses) or different concentrations or both should ensure that they include an adequate followup period in order to collect data on potential fluorosis. As it is unethical to propose RCT to assess fluorosis itself, further observational studies will necessarily be undertaken in this area. Attention does, however, need to be given to the choice of study design, bearing in mind that prospective, controlled studies will be less susceptible to bias than retrospective and/ or uncontrolled studies.

Commentary

A Cochrane systematic review that confirms the beneficial preventive effects of topical fluorides¹ was discussed on pages 6–7 of this issue. Given the strong evidence that supports the use of fluorides toothpastes, decision-makers have to balance the preventive effects with the risk of dental fluorosis. Warnings on this subject are mainly relevant to young children because they have not yet fully developed their abilities and therefore are at higher risk of swallowing toothpaste and ingesting excessive fluoride as a result.

The review here evaluates the available evidence on whether exposure to different topical fluoride treatment modalities alters the risk of developing dental fluorosis in children. It highlights the special feature of all efforts to examine the adverse effects of a certain intervention: for ethical reasons, clinical research cannot be designed to study this condition. As there is a lack of reporting the data about fluorosis in the RCT of topical fluorides, the studies that are mostly included in the review are observational studies and some of them use retrospective data. We assume some source of bias in this kind of research design, which results from the lack of random allocation to intervention. To reduce bias, the Meta-Analysis of

This paper is based on a Cochrane Review published in the Cochrane Library 2010, issue 1 (see www.thecochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Library should be consulted for the most recent version of the review.

Observational Studies in Epidemiology (MOOSE) Group agreed a checklist for critical appraisal of these studies.²

This review follows the guidelines of the Cochrane Collaboration. Two independent reviewers extracted data of the included studies. The searching was exhaustive, there were no language restrictions, there was searching of references lists and handsearching. Separate meta-analyses were carried out and the results were presented according to the different study designs because it is likely that the data from nonrandomised studies are more heterogeneous.³

The risk of bias for the two RCT included in the review is quite low, but their weaknesses do include the lack of blinding to the intervention in both studies, and unclear randomisation in one of them. Given the inherent biases associated with observational studies, none were judged to be at low risk of bias. Only one of the case–controls⁴ seems to be at low risk of bias. No information about possible confounders was available.

For the assessment of risk of bias of the cross-sectional surveys with retrospective assessment of exposure, the authors developed their own criteria. None of the studies filled all the considered criteria.

The results of two of the clinical trials are conclusive in supporting the evidence that, at higher concentrations of fluoride, the risk of fluorosis significantly increases in young children. For Holt *et al.*,⁵ who compared 550 ppm with 1000 ppm fluoride in the trial with the greater risk of bias, the RR of fluorosis in the treatment group is 75% (CI, 57–99%). For Tavener *et al.*,⁶ comparing 440 ppm and 1450 ppm fluoride, RR 0.59 (CI, 0.44–0.79).

The available evidence from observational studies is less conclusive. The two case–control studies that evaluated fluoride use at age >24 months versus ≤24 months presented contrasting results. For Osuji *et al.*,⁴ who authored the case–control study with the lower risk of bias, the risk of fluorosis was for the case group was 9% (OR, 0.09; 95% CI, 0.04–0.21) and in the Skotowski and colleagues' report,⁷ it was 70% (OR, 0.70; 95% CI, 0.3–1.6).

This review suggests that the younger the child when brushing with fluoride toothpaste is started, the greater the possibility of some fluorosis, and the higher the level of fluoride in the toothpaste the bigger the risk. Nevertheless, use of fluoride toothpaste clearly impacts upon dental caries, so there is a trade-off which will be dependent on the levels of disease in a particular community. I would suggest that, because of the levels of dental caries in most areas, the current Scottish Intercollegiate Guidelines Network⁸ to use toothpaste containing 1000 ppm fluoride (±10%) with

no more than a smear on the brush, twice per day, supervised or carried out by an adult with the child spitting out and not rinsing, and commencing after the eruption of the first deciduous tooth, would still be supportable. In areas with low disease prevalence and fluoridated water supplies there may be a need to reconsider existing recommendations.

There are clearly issues with the quality of the evidence available to address this important question. More, and higher quality, research is required both in relation to levels of fluorosis in those using topical fluorides. As many of the included studies consider mild fluorosis, and there is some evidence⁹ to suggest that mild fluorosis may not be an issue to some, further research is needed in this area to help parents and decision-makers make good decisions about when to start using fluoridated tooth paste and what level to use.

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Practice point

- This review highlights the need to be aware of the possibility of fluorosis when recommending use of topical fluoride in children aged under 6 years, and to consider the balance of the risks of caries to fluorosis risk.

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