 Prague Medical Report / Vol. 108 (2007) No. 4, p. 306–314

Is Systemic Fluoride Supplementation for Dental Caries Prevention in Children Still Justifiable?

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Received December 7, 2007. Accepted December 19, 2007.

Key words: Fluoride supplements – Fluoride intake – Dental caries prevention – Public dental health

This work was supported by the grant of IGA, Ministry of Health ČR. No. NR/8331-3.

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Abstract: Introduction of systemic and topical fluorides into the prevention and control of dental caries represents the most significant issue in dentistry in the second half of the 20th century. Fluorides have brought a considerable decline in dental caries prevalence especially in countries with advanced economies. However expanding assortment of fluoride-containing preventives and oral cosmetics has brought some concerns regarding possible adverse effects due to multiple intake sources. This review of the literature on systemic administration of fluoride supplements in the prevention of dental caries summarizes data in historical, scientific and public health retrospective. Benefits and risks of this preventive measure with special respect to possible over intake resulting in dental fluorosis are evaluated. Based on the current state of the widespread presence of fluorides in oral hygienic means and employment of topical fluoride-containing preventives the recommendation of systemic administration of fluoride supplements addresses children at increased caries risk only, over three years old and invariably in individual dosage schedule related to fluoride intake background. The decision-making on the fluoride supplements prescription to children ought to be delegated on dentists and primary care paediatricians and by no means taken as a common preventive measure in paediatric population.

Introduction

When water fluoridation was first introduced as a community based caries preventive measure in the mid-1940s it was assumed that fluoride produced most of its cariostatic effects through preeruptive effects. Ingestion of fluoride in the early years of life was thus considered essential for a full range of fluoride benefits to be achieved, and as it was assumed, the earlier in life this ingestion started, the more benefits would be achieved. Therefore it was natural, that alternative means of ingesting fluoride by infants and young children would be sought for those children who did not receive fluoridated water.

Scientific evidence now favours the efficacy of fluoride's post eruptive effects in cariostasis, which has led to a re-evaluation of the "systemic" benefits of fluoride. This review addresses fluoride supplements as one of the means of providing ingestible fluoride. Fluoride supplements were originally developed to deliver preeruptive benefits, which still play role in caries prevention in contemporary world.

Fluoride dietary supplements are manufactured as tablets or drops, intended to be swallowed, as tablets for chewing or lozenges intended to be sucked slowly or to dissolve slowly in the mouth. In this review the term "supplements" refers generically to all of the above-mentioned methods of administration.

Supplements contain a measured amount of fluoride, typically 0.25 mg, 0.5 mg, or 1.0 mg, usually as sodium fluoride, but sometimes as acidulated phosphate fluoride, potassium fluoride, or calcium fluoride. They were, and still are, intended for use only in areas where there is little or no fluoride in the drinking water, and

where there is no other or very limited intentional use of ingested fluoride. There are few data on the extent to which these products are used, but they are known to have widespread use as a caries preventive for children. In many countries, supplements are available only upon prescription, though some countries permit over-the-counter sales. In the Czech Republic both these forms are currently available. In some countries they were, and still are in some cases, distributed to children through public health programmes.

Several dosage schedules for fluoride supplementation related to the age of child appeared all over the world, which have subsequently been incorporated into the position statements and recommendations of national and supranational bodies and associations. Although the efficacy of fluoride's post eruptive cariostatic effects has evolved in more recent years, recommended schedules for supplement use in many countries have reflected this change with certain delay. Table 1, for example, shows the schedule for supplement use in five European countries including the Czech Republic at the end of 1993.

The post eruptive efficacy of fluoride supplements has been demonstrated in school-age children, though the original rationale for their use, i.e. preeruptive uptake by developing enamel to form a more resistant tooth is no longer tenable.

Some of the earliest studies on the efficacy of fluoride supplements among infants were conducted in Central and Eastern Europe, and were summarized, favourably for the most part, in extensive reviews in the 1970s [2, 3]. While it is recognized that methodically rigorous clinical trials in a paediatric population are inherently difficult, some of these studies were flawed to such an extent that their results are questionable. Flaws included the use of selected groups of participants rather than random allocation, the absence of concurrent controls, non-blinded examiners, and severe attrition of participants. The conclusions from these reviews, that supplements led to caries reductions of 50–80% in the primary dentition and 20–40% in the permanent dentition when used from birth, were likely to overestimate efficacy [1].

Well-conducted clinical trials have shown that fluoride supplements provide post eruptive cariostasis in school-age children. American studies in which the supplements were chewed, swished and swallowed by school-children under

Table 1 – Former recommended administration schedules for fluoride supplements in several European countries (mg F/day) [1].

Child's age	0–1	1–2	2–3	3–4	4–5	5–6	6+
France	0.25	0.25	0.5	0.50	0.75	0.75	1.0
Switzerland	0.25	0.25	0.5	0.50	0.75	0.75	1.0
Germany	0.25	0.25	0.5	0.75	0.75	0.75	1.0
Austria	0.25	0.25	0.5	0.50	0.75	1.00	1.0
Czech Rep.	0.25	0.25	0.5	0.75	0.75	1.00	1.0

supervision have reported caries reductions of 20–28% over 3–6 years [4, 5]. Concurrent controls, placebos, and double-blind conditions were part of the design of these studies. Caries reductions were higher for teeth erupting during the period of the study, and in one of these studies, beneficial effects were still discernible 4 years later [6]. More spectacular results, an 81.3% reduction in caries incidence, were reported from a study in Glasgow, Scotland, in which children initially aged 5.5 years from lower socioeconomic groups sucked a 1.0 mg fluoride tablet, or a placebo, under supervision in schools every school day for 3 years [7]. The benefits were almost entirely seen in the erupting permanent first molars.

The results from retrospective analyses of supplement use provide weaker evidence than clinical trials, and results of such studies have been confusing Positive results from the use of supplements have been reported from Britain, New Zealand, The Netherlands, Australia, Switzerland, and Sweden [8, 9]. Retrospective studies are easily biased by self-selection of supplement users, and such bias was evident in all of these studies. The problem that arises is that cause-and-effect cannot be judged. The favourable results may have come from use of the supplements, or they may have been seen anyway because of the dental awareness of the families choosing to use supplements. Even with the biasing effects of self-selection, there are other evaluation studies, which found no difference in caries experience between those children who reported using fluoride supplements and those who did not [10, 11, 12, 13, 14].

There have been well-conducted clinical trials, in which fluoride supplements were tested in combination with other fluoride therapies in school-based studies. Driscoll and colleagues [15] found that supplements used with the swish-and-swallow procedure over 8 years, gave slightly better results than fluoride mouth rinsing, though caries increments in all study groups were small. In Scotland, no difference in caries incidence was found over 6 years among three groups of children using fluoride supplements, mouth rinse, and combinations of both with placebo [16]. A Swedish study comparing supplements, fluoride toothpaste, and fluoride varnish could find no difference among the groups [17].

Evidence of an efficacy of any preventive procedure should come, as far as possible, from clinical trials, which meet specific quality criteria. Only a handful of fluoride supplement trials meet these standards. The evidence from these trials is that supplements are effective when used with school-age children, and when the supplements were used topically by chewing or slow dissolution in the mouth. There is little satisfactory evidence for the efficacy of fluoride supplements when used from birth or early infancy.

Supplements and risk of fluorosis

What has come to be called the "critical period" for the development of fluorosis is the late secretion-early maturation period of preeruptive dental enamel. While

fluorosis can develop at any stage of preeruptive development under certain conditions, in this critical period the developing enamel is especially sensitive to ingested fluoride [18, 28].

There have been some reports, in which no association was found between supplement use and the development of fluorosis [10, 19]. The fluorosis found among the 322 children in one of these studies [10] was attributed to the swallowing of fluoride toothpaste rather than to the supplements. On the other hand, there is a substantial literature, in which fluorosis has been associated with supplement use. A number of case studies also reported fluorosis among patients who ingested 0.5 mg or 1.0 mg of fluoride supplements daily from infancy [19].

Probably the strongest evidence to show that fluoride supplements are a risk factor for fluorosis, especially when ingested during the critical period of late secretion-early maturation, came from the case-control study of [20] that found a mild-to-moderate enamel fluorosis being strongly associated with fluoride supplementation during the first six years of life (odds ratio = 4.0) and with median household income (odds ratio = 6.6). Subjects in the middle median household income group who had used fluoride supplements through the first six years of life had a 28-fold increase in the risk of fluorosis compared with unexposed subjects in the lower median household income group. To sum up, the evidence is clear that fluoride supplements, when ingested prior to tooth eruption, are a risk factor for dental fluorosis.

Ingested fluoride from multiple sources during first few years of life constitutes the problem of dental fluorosis. The amount of fluoride in early childhood, which would lead to fluorosis, was originally estimated to be 0.1 mg F/kg body weight/day [21]. Since then this estimate has been revised downward, with 0.03 F/kg body weight/day being the lowest suggested limit [22].

At the time when the preeruptive fluoride intake was considered to be a primary mode of fluoride action, the ingestion of fluoride in the range of 0.05–0.07 mg F/kg body weight/day was considered "optimal" for preeruptive caries prevention [23]. In the light of present knowledge that preeruptive fluoride has little preventive effect, this range is rather used as an estimate of the maximum amount to be ingested by young children if fluorosis should be maximally reduced.

In some parts of Europe a similar situation may exist, for while the children may ingest less fluoride from food and drink because of the absence of fluoridated water during the food processing, they may get more fluoride from high-concentration toothpastes. Where 0.4–0.6 mg F/day is being ingested by a child under 3 years of age, regardless of the source of fluoride, it is likely to be enough to cause fluorosis. Adding more fluoride from the supplements would only make the problem worse while adding no cariostatic benefits. When considering the risk/benefit ratio of fluoride supplements, total fluoride ingestion from all sources must be kept in mind.

Fluoride toothpastes

Fluoride toothpastes were introduced in the late 1960s and early 1970s and their rapid and remarkable increase on the market share was followed by massive reduction in dental caries seen in many countries during the 1970s and 1980s [24, 25]. A considerable body of evidence in the literature on the role of fluoride toothpastes in the worldwide caries decline evaluated by the World Health Organization, Fédération Dentaire Internationale and other supranational and national scientific bodies has lead to reappraisal of the systemic administration of fluorides. A mild increase in the prevalence of enamel developmental defects known as dental fluorosis accompanying the caries decline [30, 31] indicating a possible over dosage of fluoride in the childhood during the enamel development supported the necessity of this re-evaluation of systemic fluoride supplementation. It was done in 1991 in a meeting in Brussels entitled "European view of fluoride supplementation". This meeting addressed dosage of different products and age-related dose recommendations for fluoride supplements throughout Europe leading to considerable confusion in a more integrated Europe with its mobile and multilingual society. The panel of experts has reached a consensus on the necessity 1) to indicate fluoride tablets administration strictly as a supplement to the background fluoride intake from food, 2) to start with fluoride supplementation (if necessary) at the age of three years and 3) to take fluoride supplementation by no means as a wide spread preventive measure [26].

Many dentists around the world however hold firm beliefs about the value of fluoride supplements ingested from birth. But the evidence to support the use of supplements from birth is limited. Assuming that there is little preeruptive efficacy, a reasonable choice regarding supplements use is to start no earlier than with the eruption of the primary molars, or during the third year of life.

Enamel opacities seen in permanent teeth associated with the use of supplements in young children represents the mildest form of the fluorosis Claims of dentists have no public health significance. These arguments date back to the middle decades of the 20th century when severe caries involvement among children was common, but it may not be applicable in contemporary conditions, and it can be dangerous for dental professionals to make judgments as to what is or is not aesthetic. There is now evidence that the public may be more aware of very mild fluorosis than have previously been imagined [19, 27, 28, and 32].

Reappraisal of fluoride supplements administration schedule

Increased apprehensions of the fluorosis risks have lead many European national paediatric and dental societies to the reappraisal of the child's age suitable for the onset of fluoride supplements administration and the respective schedules related to the background fluoride intake from food and oral hygiene means.

At the beginning of a new millennium the Czech Paediatric and Dental Societies adopted a consensus statement regarding fluoride supplements with a

considerable narrowing of indication criteria and reducing the administration schedules (Table 2) [34].

Current view of fluoride supplement usage

It is possible that slow dissolution fluoride lozenges may start to play role in caries control in older children and adults, i.e. persons who are no longer at risk of enamel fluorosis. The intention is that the supplements will help maintain certain levels of fluoride in the oral cavity, which is the main goal for the fluoride use in caries prevention. The future of fluoride supplements can be seen in tablets or chewing gums slowly releasing fluorides for children from the age when they are able to retain them in the mouth for a longer period of time. The benefit of such fluoride supplements used in the above-described way still needs to be investigated.

Anyway, there are other existing methods, mostly utilizing fluoride in toothpastes or mouth rinses, of maintaining the appropriate fluoride level in the oral cavity. Fluoride supplements are inappropriate for public health use in most countries, and if used at all, they should be restricted to individual patients older than 7 years with severe caries.

For all the above-mentioned reasons the fluoride supplements should not be thought of as dietary supplement that will automatically protect against caries by delivering added benefits but rather as a supplement to "inadequate water and food content of fluoride". This is not the case. To be effective against caries fluoride supplements should be thought of as a means to support the topical mechanisms of fluoride action and not the systemic action of fluoride. This was illustrated very clearly by Stephen and co-workers [7] who provided fluoride tablets to children in Scotland to either swallow or hold in the mouth (sucking or chewing). The group that dissolved the fluoride in the mouth and thereby "applied" fluoride topically had dramatic caries reductions (approximately 80%) in comparison to the tablet swallowers. If used, then fluoride supplements should be prescribed with instructions to chew or suck in order to provide a caries-protective benefit.

Table 2 – Newer recommended administration schedule for fluoride supplements [34].

Age	½–3 yrs		3–6 yrs		6+ yrs
Regular tooth cleaning with F tooth paste	F tooth paste no	yes (since 2 yrs)	F tooth paste no	yes	F tooth paste yes
Fluoride content in water	Daily dose of tablets (0.25 mg F)				
< 0.3 mg/l	1	0	2	1	4
0.3–0.6 mg/l	0	0	1	0	2
> 0.7 mg/l	0	0	0	0	0

It has been suggested that when fluoride tablets are swallowed, the fluoride returned via the plasma to the saliva may be sufficient to provide a "topical" benefit. Examination of work by Ekstrand and co-workers [28] shows that after ingestion of a fluoride tablet only a transient elevation of plasma fluoride occurs and that its salivary levels resulting from ingestion of fluoride tablet once daily are unlikely to have much, if any, topical benefit. This further supports the need to use fluoride supplements directly as a topical fluoride delivery mechanism if they are to be effective [29].

Summary and conclusions

The anti-caries effects of fluoride are primarily topical for children and for adults. The mechanisms of action of fluoride include the inhibition of demineralization on crystal surfaces, enhancement of remineralisation on crystal surfaces, and inhibition of bacterial activity. Systemic benefits of fluoride are minimal. Therapeutic levels of fluoride can be achieved in drinking water and by topically applied fluoride products. If used, fluoride supplements should be employed as a topical delivery system by chewing or sucking tablets or lozenges for a maximum possible time before swallowing [29, 33].

References

1. BURT B. A., MARTHALER T. M.: Fluoride tablets, salt fluoridation and milk fluoridation. In: Fluoride in dentistry. Fejerskov O., Ekstrand J., Burt B. A. (eds), Munksgaard, Copenhagen, 1996, 291–310.
2. AASENDEN R., PEEBLES T. C.: Effects of fluoride supplementation from birth on deciduous and permanent teeth. *Arch. Oral Biol.* 19: 321–326, 1974.
3. BINDER K., DRISCOLL W. S., SCHÜTZMANNSKY G.: Caries-preventive fluoride tablet programs. *Caries Res.* 12: 22–30, 1978.
4. DEPAOLA P. F., LAX M.: The caries-inhibiting effect of acidulated phosphate-fluoride chewable tablets: a two-year double-blind study. *J. Am. Dent. Assoc.* 76: 554–557, 1968.
5. DRISCOLL W. S., HEIFETZ S. B., KORTS D. C.: Effect of chewable fluoride tablets on dental caries in schoolchildren: results after six years of use. *J. Am. Dent. Assoc.* 97: 820–824, 1978.
6. DRISCOLL W. S., HEIFETZ S. B., BRUNELLE J. A.: Cariespreventive effects of fluoride tablets in schoolchildren four years after discontinuation of treatments. *J. Am. Dent. Assoc.* 103: 878–81, 1981.
7. STEPHEN K. W., CAMPBELL D.: Caries reduction and cost benefit after 3 years of sucking fluoride tablets daily at school. A double-blind trial. *Br. Dent. J.* 144: 202–206, 1978.
8. LIMBACK H.: A re-examination of the pre-eruptive and post-eruptive mechanism of the anti-caries effects of fluoride: is there any anti-caries benefit from swallowing fluoride? *Community Dent. Oral Epidemiol*. 27: 62–71, 1999.
9. RIORDAN P. J.: Fluoride supplements in caries prevention: a literature review and proposal for a new dosage schedule. *J. Public Health. Dent*. 53: 174–189, 1993.
10. BAGRAMIAN R. A., NARENDRAN S., WARD M.: Relationship of dental caries and fluorosis to fluoride supplement history in a non-fluoridated sample of schoolchildren. *Adv. Dent. Res.* 3: 161–167, 1989.
11. FRIIS-HASCHE E., BERGMANN J., WENZEL A., THYLSTRUP A., PEDERSEN K. M., PETERSEN P. E.: Dental health status and attitudes to dental care in families participating in a Danish fluoride tablet program. *Community Dent. Oral. Epidemiol.* 12: 303–307, 1984.

12. HOLM A. K., ANDERSSON R.: Enamel mineralization disturbances in 12-year-old children with known early exposure to fluorides. *Community Dent. Oral Epidemiol.* 10: 335–339, 1982.
13. KALSBEEK H., VERRIPS E., DIRKS O. B.: Use of fluoride tablets and effect on prevalence of dental caries and dental fluorosis. *Community Dent. Oral Epidemiol.* 20: 241–245, 1992.
14. THYLSTRUP A., FEJERSKOV O., BRUUN C., KANN J.: Enamel changes and dental caries in 7-year-old children given fluoride tablets from shortly after birth. *Caries Res.* 13: 265–76, 1979.
15. DRISCOLL W. S., NOWJACK-RAYMER R., SELWITZ R. H., LI S. H., HEIFETZ S. B.: A comparison of the cariespreventive effects of fluoride mouthrinsing, fluoride tablets, and both procedures combined: final results after eight years. *J. Public Health Dent.* 52: 111–116, 1992.
16. STEPHEN K. W., KAY E. J., TULLIS J. I.: Combined fluoride therapies. A 6-year double-blind schoolbased preventive dentistry study in Inverness, Scotland. *Community Dent. Oral Epidemiol.* 18: 244–248, 1990.
17. PETERSSON L. G., KOCH G., RASMUSSON C.,G., STANKE H.: Effect on caries of different fluoride prophylactic programs in preschool children. A two year clinical study. *Swed. Dent. J.* 9: 97–104, 1985.
18. BROUKAL Z.: Kritická perioda vývoje skloviny stálých zubů (Critical period of the enamel development in permanent dentition). *Prakt. Zub. Lék.* 48: 35–38, 2000.
19. ISMAIL A. I.: Fluoride supplements and fluorosis: a meta-analysis. *Community Dent. Oral Epidemiol.* 27: 48–56, 1999.
20. PENDRYS D. G., KATZ R. V.: Risk of enamel fluorosis associated with fluoride supplementation, infant formula, and fluoride dentifrice use. *Am. J. Epidemiol.* 130: 1199–1208, 1989.
21. FORSMAN B.: Early supply of fluoride and enamel fluorosis. *Scand. J. Dent. Res.* 85: 22–30, 1977.
22. FEJERSKOV O., STEPHEN K. W., RICHARDS A., SPEIRS. R.: Combined effect of systemic and topical fluoride treatments on human deciduous teeth – case studies. *Caries Res.* 21: 452–459, 1987.
23. OPHAUG R. H., SINGER L., HARLAND B. F.: Estimated fluoride intake of average two-year-old children in four dietary regions of the *United States. J. Dent. Res.* 59: 777–781, 1980.
24. MARTHALER T. M.: Changes in dental caries 1953–2003. *Caries Res.* 38: 173–81, 2004.
25. CLARKSON J.: A European view of fluoride supplementation. *Br. Dent. J.* 172: 357, 1992.
26. CLARK D. C., HANN H. J., WILLIAMSON M. F., BERKOWITZ J.: Aesthetic concerns of children and parents in relation to different classifications of the Tooth Surface Index of Fluorosis. *Community Dent. Oral Epidemiol.* 21: 360–364, 1993.
27. EKSTRAND J.: FLUORIDE METABOLISM. In: Fluoride in dentistry. Fejerskov O., Ekstrand J., Burt B. A. (eds), Munksgaard, Copenhagen, 1996, 55–68.
28. FEATHERSTONE J. D. B.: Prevention and reversal of dental caries: role of low level of fluoride. *Community Dent. Oral Epidemiology* 27: 31–40, 1999.
29. WHELTON H. P., KETLEY C. E., MCSWEENEY F., O'MULLANE D. M.: A review of fluorosis in the European Union: prevalence, risk factors and aesthetic issues. *Community Dent. Oral Epidemiol.* 32: 9–18, 2004.
30. LEVY S. M., MCGRADY J. A., BHURIDEJ P., WARREN J. J., HEILMAN J. R., WEFEL J. S., FACTORS PETERSSON G. H., BRATTHALL D.: The caries decline: a review of reviews *Eur. J. Oral Sci.* 104: 436–443, 1996.
31. BRATTHALL D., HÄNSEL-PETERSSON G., SUNDBERG H.: Reasons for the caries decline: what do the experts believe? *Eur. J. Oral Sci.* 104: 416–422, 1996.
32. PETERSEN P. E., LENNON M. A.: Effective use of fluorides for the prevention of dental caries in the 21st century: the WHO approach. *Community Dent. Oral Epidemiol.* 32: 319–321, 2004.
33. NEVORAL J., JANDA J., FRÜHAUF P., BROUKAL Z., MERGLOVÁ V., HANDZEL J., CABRNOCHOVÁ H. ET AL.: Fluoridy v prevenci zubního kazu u dětí. Stanovisko České pediatrické společnosti ČLS JEP, České společnosti pro dětskou stomatologii a Odborné společnosti praktických dětských lékařů (Fluorides in prevention of dental caries in children. Consensus statement of Czech paediatric and Dental Societies) *Čes.-slov. pediat.* 58: 89–90, 2003.