Recommendations for the Use of Fluoride in Caries Prevention

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Summary: From a theoretical point of view, caries can be prevented by perfect oral hygiene and sugar abstinence. However, practice has shown that this approach is successful in individual cases only. For the whole population, effective caries prevention is still not realistic without the use of fluoride in various forms. The use of different fluoride preparations increases its efficacy. On the other hand, correct dosage is important to prevent the risk of dental fluorosis. Most of the European scientific dental associations no longer recommend the use of fluoride supplements, such as fluoride tablets or drops, as a standard procedure in caries prevention. This is due to the increasing evidence that the effect of fluoride is mainly the result of chemical reactions on the tooth surface. Therefore, fluoridated toothpastes, gels, varnishes, and rinses are more in focus. Besides this, fluoridated water and fluoridated salt are still important. Although they have a systemic effect, the efficacy of these fluoride applications results from local processes.

Key words: fluoride, caries

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Etiology of caries may be regarded as general knowledge in industrialized countries. As a matter of principle, it is possible to fight the disease by avoiding ingestion of sugar or by applying perfect oral hygiene. However, in practice this seems extraordinarily difficult. Scientific examinations and practical experiences showed repeatedly that a significant reduction of sugar consumption and perfect oral hygiene cannot be attained in wide sections of the population (Marthaler, 1990; Micheelis and Schroeder, 1999; Bauch et al, 1991). Therefore, for the population a regular supply of fluoride is the most important measure in caries prevention to strengthen the resistance of dental hard tissues. For a long time, the systemic effect of fluoride was regarded to be most important, resulting in recommendations to use fluoride supplements such as tablets or drops. However, there is increasing evidence that the local effect of fluoride at the surface of erupted teeth is by far more important. Therefore this focus article discusses actual European recommendations for the use of fluoride in caries prevention.

FLUORIDE – ITS VALUE TO MAN

Fluorides are chemical compounds of fluorine and organic or anorganic cations. Fluoride can be found everywhere in nature in soil, air, and water, either as lightly soluble salts (sodium- or potassium fluoride) or as barely soluble minerals (fluorite or fluorapatite). Fluoride is a natural element within the fauna and flora and their food chain. In this context it is also absorbed into the human body (Smith and Ekstrand, 1988). Fluoride is regarded as an important trace element, which has a high impact on growth of bone and teeth because it serves as core of mineralization (Karlson, 1984). It is mainly ingested with food and 90% is absorbed. Approxi-

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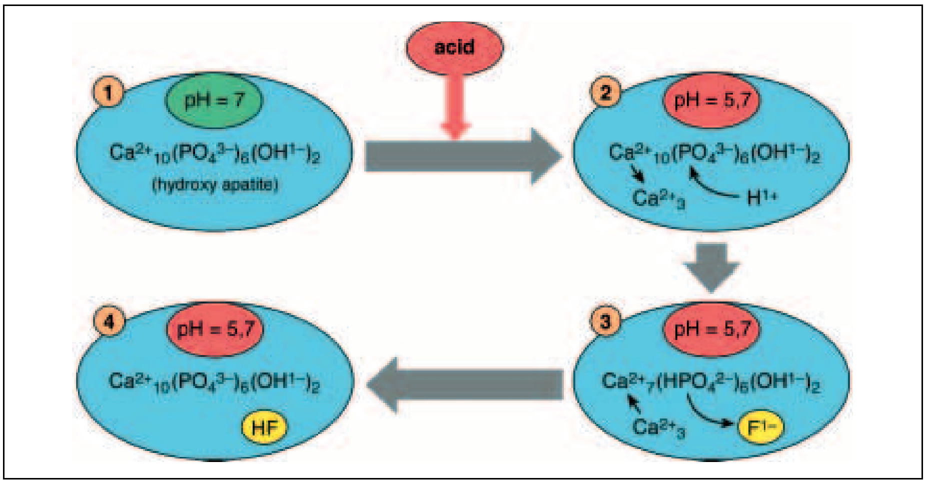

Fig 1 Phosphate (PO_4^{3-}) from the hydroxyapatite (1) is protonated by H^+-Ions if the ph drops below 5.7 (2). Hence, the phosphate molecule loses one negative charge, which is important to bind calcium ions (Ca^{2+}). This causes a loss of calcium. Fluoride can inverse this process even if the ph remains low. Because of its strong electro negativity it can bind on the H^+-Ion therefore eliminate it from the enamel (3, 4).

mately half is estimated to be eliminated via urine, less in children, more in adults. 99% is incorporated into bone and teeth (Ekstrand and Whitford, 1988), the rest is spread over the other tissues. In total, an adult human body contains about 2.6 g of fluoride (Hopfenzitz, 1996). According to its primary location in bone and teeth fluoride has a major impact on the stability of bone and it has a leading role in caries prevention.

CARIES PREVENTIVE MECHANISMS OF FLUORIDE

The action of fluoride is based on chemical and possibly on antibacterial effects. The chemical effect is the most important and will be discussed more in detail than the antibacterial effect.

Chemical Action of Fluoride

From a chemical point of view, a tooth may be regarded as a barely soluble salt (enamel and dentine) which is exposed to an aqueous solution (saliva). Ideally, there is a well-balanced equilibrium between de- and remineralization. However, this balance is lost when dental plaque and sugar is frequently present in the oral cavity. In such a case demineralization will prevail due to acidic metabolites from bacteria. This will first result in microscopically detectable carious lesions with characteristic appearance (subsurface lesion) which later will merge into cavities. Demineralization is initiated by protonation of phosphate in apatite of enamel and/or dentine (PO_4^{3-} + H^+ (HPO_4^{2-}) (Fig 1). Calcium will therefore not be bound to an adequate extent but rather will be lost (König 1987). On the other hand the presence of fluoride promotes the opposite reaction catalyzing remineralization using the calcium of saliva and thus reverses the loss of substance before it can be detected microscopically. Furthermore, lesions which are already visible as white spots and already spread into dentine can be remineralized and healed with fluoride (Itthagarun et al, 2000; ten Cate, 2001; Wefel et al, 1995). On a molecular basis, fluoride is capable of removing protons (H^+-ions) from the demineralized hard tissues which allows a re-embedding of calcium (König, 1987) (Fig 1). In an acidic solution, ten Cate and Duijsters could show a dose-response relationship between the concentration of fluoride and the calcium loss of enamel specimens (ten Cate and Duijsters, 1983).

Another yet less important action of fluoride is the stabilization of the present hard tissues. Apatite in enamel and dentine is chemically not a pure hydroxy-apatite ($Ca_{10}(PO_4)_6(OH)_2$). Amongst other, there is a constant lack of OH-ions. These 'vacancies' within the crystalline structure can be occupied by fluoride. This will result in fluoridated apatite ($Ca_{10}(PO_4)_6(OH)F$) or ideally in a fluor-apatite ($Ca_{10}(PO_4)_6F_2$), both of which are more stable against acidic attacks. However, under in vivo conditions, fluor-apatite develops rather scarcely (König, 1987; Featherstone and ten Cate, 1988; ten Cate, 1979). Moreno et al detected fluoride replacement of OH–ions in less than 10% of the outer surface of enamel; at a depth of 50µm it was only 1% (Moreno et al, 1977).

Antibacterial Action of Fluoride

Fluoride hampers the carbohydrate metabolism of streptococcus mutans by incorporating fluoride as hydrofluoric acid (HF) and therefore cytoplasmatic acidification (Whitford et al, 1977). This results in a non-specific inhibition of the glycolysis because several enzymes including enolase have their optimum efficacy in a neutral environment. Moreover the sugar transport system is sensitive to acidification of the cytoplasma (Belli and Marquis, 1994). Both mechanisms reduce the generation of energy in the bacterial cell and the production of lactate (Hamilton and Bowden, 1988; Loveren van, 2001). However, the antibacterial effect of fluoride is of inferior importance unless the fluoride is not bound to cations which have their own specific antibacterial activity. It is even not yet clearly proven to be existent under in vivo conditions (Loveren van, 2001).

Systemic and Local Effect of Fluoride

For years, the major caries-preventive effect of fluoride has been ascribed to its ability to form fluor-apatite. Based on this comprehension, systemic fluoride (practiced mostly through daily tablet intake) was favored on the assumption that this would result in internal formation of fluor-apatite before teeth were exposed to an oral environment. This would make teeth resistant to carious attacks on a long-term basis. This concept was disproved in *in vitro* studies using shark teeth. Those teeth are built from pure fluor-apatite with a fluoride concentration of 32,000 ppm. Ögaard et al compared the solubility of these teeth with human enamel in vitro. In their study, the human enamel showed a fluoride concentration of 1,270 ppm at the surface, which decreased rapidly in the central areas of enamel (Ögaard et al, 1988). On the comprehension that 'indestructible' enamel containing a high amount of fluor-apatite, it should have been impossible to create carious lesions in shark teeth. However, it has been shown that in an *in vitro* caries model, shark teeth developed lesions with almost similar depth and mineral loss as human teeth (Ögaard et al, 1988). These findings reinforce the understanding that the beneficial action of fluoride depends much more on its ability to enhance remineralization than on its ability to form stable apatite and thus resist acidic attacks. The lack of benefit of pre-eruptive systemic fluoride application has been shown by Reich et al, who performed a prospective study in newborn children. The authors demonstrated that there was no difference in caries development at the age of five years if fluoride was administered as tablets right after birth as opposed to an application starting in the age of seven months, i.e. with the eruption of the first deciduous tooth (Reich et al, 1992).

Increasing knowledge about the importance of fluoride in the process of de- and remineralization has lead to the fact that topical application of fluoride is preferred to the systemic one (Riordan, 1999; Limeback, 1999; DGZMK, 2000). However, it has to be taken into consideration that every systemic intake of fluoride also has a topical aspect if there are already teeth in the oral cavity: Firstly, during its passage through the mouth (e.g. as fluoridated salt) it will have local contact to the teeth; Secondly, after its resorption in the gastro-intestinal tract it will gain access to the blood circulation and to the saliva. In this manner, fluoride is locally available in low concentrations but over a relatively long time period. In vitro studies have shown that concentrations of 0.1 ppm may already be effective for caries prevention (ten Cate and Duijsters, 1983; Amjad and Nancollas, 1979). If food had been prepared with fluoridated salt at 250 ppm the above mentioned or even higher concentrations can be measured in saliva during and after its ingestion (Macpherson and Stephen, 2001; Hetzer and Korn, 1997; Sjögren and Birkhed, 1993).

TOXICOLOGICAL ASPECTS

Compared to other substances which are regularly ingested by humans, fluoride has a high therapeutic safety. The lethal dose ranges between 32 and 64 mg F-/kg body weight (Hodge and Smith, 1965) which would imply 3,500 mg F- (3.5 mg) for an adult of 75 kg. Other sources even report lethal doses of 5,000–10,000 mg (5–10 g) in adults (Mühlendahl et al, 1995). The German society for nutrition recommends a daily fluoride intake of about 3.5 mg for an adult (Przyrembel, 1998). Therefore the factor between recommended and lethal dose is at least 1,000. In contrast, the lethal dose for sodium chloride which is usually consumed in an amount of 8-10 g/day is 40-75 g for an adult. This is less than the ten fold of the average daily ingested amount (Mühlendahl et al, 1995).

For practical purposes the knowledge about the lethal dose of fluoride is not very helpful. More important is the question: Which dose will lead to first undesired effects? The toxicological assessment of any substance has to be assessed on a dose-related basis. The ingested amount of the substance and the body weight of the patient has to be known as well as the sensitivity of humans against the substance. Also, there needs to be a distinction between chronic and acute toxicity. Acute toxicity describes the immediate toxic effects after one single ingestion whereas the chronic toxicity relates to effects which appear slowly as a consequence of slight over dosage over a long period.

Acute Toxicity

The minimal fluoride dose which may cause toxic signs and symptoms and which requires an immediate therapeutic intervention is found to be 5 mg/kg body weight. It is defined as probably toxic dose (PTD) (Whitford, 1996). For example, there is a risk of toxic signs if a six-year-old child with a body weight of 20 kg has ingested the whole content of a tube of toothpaste with 1,500 ppm F- (75 ml with 112.5 mg F-). For fluoridated salt, the PTD is reached if this child ingests 400 g of salt. However, the lethal dose of sodium chloride for a child of this age is about 15–20 g (Mühlendahl et al, 1995).

Chronic Toxicity

If fluoride is ingested in elevated doses over longer time-periods, changes in teeth and bone can result. These changes are called fluorosis. In teeth, they are the result of some disturbance in mineralization, resulting in a higher organic proportion. Dental fluorosis can only occur during tooth formation. In contrast, fluorosis of the bones is the result of an overmineralization and can occur during the entire life. First signs of skeletal fluorosis can be observed after the ingestion of more than 10 mg F-/day over a period of at least 10 years. These changes do not have any impact on health (Whitford, 1996). Because of dose and exposure time, fluoride containing caries preventive agents cannot be considered as risk factor for skeletal fluorosis. However, already a slight overdose of fluoride during tooth formation may result in a dental fluorosis. The primary effects occur during the early maturation stage of enamel (Evans and Stamm, 1991; DenBesten and Thariani, 1992; DenBesten, 1999; Zhou et al, 1996; Lyaruu et al, 1987; DenBesten et al, 1985). It is not possible to define a threshold value for the formation of dental fluorosis. In the literature, values between 0.03 and 1.0 mg F-/kg body weight and day can be found (Mascarenhas, 2000). A fluoride uptake between 0.05 and 0.07 mg F-/kg bodyweight and day is regarded as optimal (Villa et al, 1999). Recommendations for the use of fluoride in caries prevention have always to be based on the best compromise between preventive efficacy and fluorosis risk. Since there are individually varying predisposing factors for fluorosis (Mascarenhas, 2000) and since it is not possible to exactly determine the individual fluoride uptake, it has to be considered that an effective caries prevention with fluoride is always associated with a slight prevalence of mild fluorosis. In the US an increase of fluorosis is reported (Pendrys and Stamm, 1990; Clark, 1994). In Europe the situation varies among the different countries. An increase in fluorosis was shown in Belgium (Carvalho et al, 2001), whereas a low fluorosis level and no increase was found in France, Great Britain, and Germany (Dünninger and Pieper, 1991; Einwag, 1993; Reich and Beermann, 1996; Obry-Musset, 1998; Holloway and Ellwood, 1997). Except for its severe forms which show large enamel defects (Thylstrup and Fejerskov, 1978) (Fig 2), fluorosis is an issue of at most esthetical concern. Interestingly, a study in Great Britain showed that mild forms of dental fluorosis (TF-index 1 and 2 (Thylstrup and Fejerskov, 1978)) are not considered to be esthetically disturbing. On the contrary, its perception is rather positive (Hawley et al, 1996). The risk of the formation of dental fluorosis on anterior teeth ends at the age of six years, because only posterior teeth, second premolars and particularly second molars are not fully mineralized at this age.

Fig 2 Severe fluorosis (TF-Index grade 7)

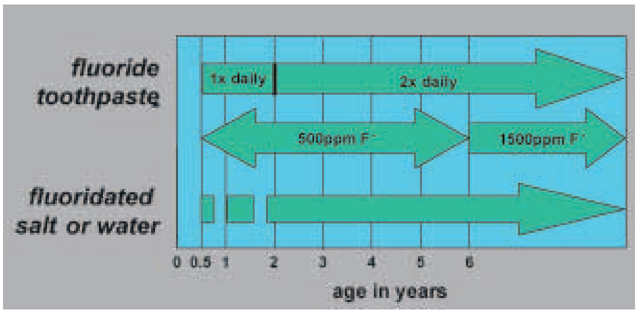

Fig 3 Fluoride timetable

RECOMMENDATIONS FOR THE USE OF FLUORIDE

The multiple use of various fluoride products leads to an increased protection against caries. Fig 3 shows a fluoride timetable that is based on the guidelines of the European Academy of Paediatric Dentistry (EAPD) and the German Dental Association (DGZMK) (DGZMK, 2000; Oulis et al, 2000). The adherence to these recommendations will provide good caries prevention with a low risk of fluorosis only. The recommendations are based on the principle that only one type of systemic fluoride should be applied. According to the guidelines from the DGZMK, supplements are only indicated for children who are deemed to be at increased caries risk and do not use fluoride toothpaste or fluoridated salt.

The guidelines are based on the finding that the local effect of fluoride is far more influential than the systemic one (Featherstone, 1999). Apparently, a caries preventive effect on unerupted teeth does not exist (Reich et al, 1992). Therefore, from a caries preventive viewpoint it makes no sense to provide children with fluoride before the first tooth appears in the oral cavity. On erupted teeth, the so called systemic fluoridation has some beneficial effect. However, this is not based on a systemic but local effect, for example if food with fluoridated salt or water is chewed. The fluoride uptake of infants from fluoridated salt or water is low and therefore, the benefit from these fluoride sources may be small. But on the other hand, the entire population will benefit from these fluoride sources and therefore, the use of fluoridated water or salt can be considered as an important public health measure.

It is recommended that children up to the age of six years should use a toothpaste with reduced fluoride content (500ppm) (DGZMK, 2000; Oulis et al, 2000). The use of this toothpaste should start with the eruption of the first deciduous tooth. A pea-sized amount should be used once, and from the second birthday on a twice daily basis. Starting with the sixth birthday, a ‘normal’ toothpaste with 1,500ppm fluoride should be used. If an increased caries protection is required, e.g. at high caries risk, a highly concentrated fluoride gel (12,500ppm F-) can be used weekly. Alternatively, fluoride mouth rinses with 200–500ppm F- can be used on a daily basis. Both preparations are not recommended for children under the age of six.

CONCLUSION

Since the main effect of fluoride results from reactions at the tooth surface, it should only be applied if teeth are already present in the oral cavity. This means that fluoride prevention should start with the erupting first deciduous tooth. The combination of various forms, e.g. fluoridated salt, toothpaste, and gel enhances the effect of fluoride. If properly used it can be considered as effective and safe.

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