Caries-inhibitory effect of titanium tetrafluoride in rats

Liv Skartveit, Carl-Johan Spak, Anne Bjørg Tveit and Knut A. Selvig
Department of Dental Research and Department of Cariology and Endodontics, School of Dentistry, University of Bergen, Bergen, Norway, and Department of Cariology, School of Dentistry, Karolinska Institute, Stockholm, Sweden

Skartveit L, Spak CJ, Tveit AB, Selvig KA. Caries-inhibitory effect of titanium tetrafluoride in rats. Acta Odontol Scand 1991;49:85–88. Oslo. ISSN 0001–6357.

The purpose of this study was to evaluate the caries-inhibitory effect of TiF_4 as compared with equimolar solutions of neutral and acidified NaF. Sixty Sprague–Dawley rats were weaned 19 days after birth and given a cariogenic diet. They were randomly divided into four groups and given a 1-min topical treatment of the molar teeth on day 1 and day 17 of the experiment with the following solutions: group 1: 1% TiF_4, pH 1.5; group 2: 1.3% NaF, pH 7.0; group 3: 1.3% NaF, pH 1.5; and group 4: control, distilled water. From day 2 the rats were inoculated with *Streptococcus mutans* twice weekly. On day 55 the rats were killed, and caries scored in accordance with Keyes. Total caries scored were (mean ± SD): group 1, 12.7 ± 9.5; group 2, 17.4 ± 8.6; group 3, 14.3 ± 9.7; and group 4, 29.5 ± 9.0. There were significantly ($p < 0.05$) reduced caries scores for total caries and for buccal + lingual and sulcal areas for all test groups as compared with the control group. Differences between control and test groups in proximal surfaces and between fluoride groups were non-significant. The results showed that the caries-inhibitory effect of TiF_4 is at least as good as that of NaF in rats. □ *Animal study; preventive dentistry; topical fluoride application*

Liv Skartveit, Department of Dental Research, University of Bergen, Aarstadveien 17, N-5009 Bergen, Norway

In comparison with various other fluoride compounds used for topical application to tooth surfaces, titanium tetrafluoride (TiF_4) has shown some interesting effects. A 4-min topical application of a 3.4% solution in vitro results in a fluoride uptake in enamel and root surfaces similar to that from fluoride varnishes and much higher than from a 2% NaF solution (1–3). The concentration of the TiF_4 solution can be reduced to 1% (0.32 M F) and the application period to 10 sec, and the TiF_4 still gives a substantial fluoride uptake in root surfaces (4). An in vivo study in dogs has shown that after a 10-sec application of 1% TiF_4, large amounts of fluoride remain in the dentin surfaces after 22 weeks of exposure to intraoral conditions (5). Topical application of TiF_4 results in reduction of enamel solubility and inhibition of artificial lesion formation (3, 6, 7). In a clinical trial in which an annual application of TiF_4 was compared with the effect of acidulated phosphate fluoride (APF), TiF_4 showed the best caries-prophylactic effect after 3 years (8).

In rats the caries-inhibiting effect of TiF_4 has been found to be similar to that of NaF (6). In that study the fluoride agents, both containing 0.2%F, were applied daily for 5 days before a 10-day cariogenic period.

The purpose of the present study was to assess the caries-inhibitory effect of TiF_4 as compared with an equimolar solution of NaF when applied under a regimen more similar to clinical procedures. Thus, the fluoride agents were applied twice during the experimental period, and an extended cariogenic period was chosen. An acidified NaF solution, adjusted to the same pH as native TiF_4 (pH 1.5), was also included in the comparison.

Materials and methods

Sixty Sprague–Dawley rats were taken from their dams and weaned on day 19 after birth. They were given a fluoride-free, carcinogenic diet containing 56% sucrose (9), and de-ionized water ad libitum. The following

day, day 1 of the experiment, the rats were randomly divided into four groups, which were assigned to the following topical treatments: group 1: 1% $TiFa_4$ (0.32 M F), pH 1.5; group 2: 1.3% NaF (0.32 M F), pH 7.0; group 3: 1.3% NaF (0.32 M F), pH 1.5; and group 4: control, distilled water.

Test and control solutions were applied for 1 min to the molar teeth with a cotton swab saturated with fluid. The treatments were repeated on day 17.

On day 2 of the experiment all rats were inoculated orally with *Streptococcus mutans*, strain E 49. Inoculation was repeated twice weekly throughout the experimental period, and the level of infection was confirmed by taking oral bacterial samples for culturing regularly. The rats were housed in stainless steel, screen-bottom cages. They were weighed weekly, and their physical condition noted. After 55 days the animals were killed in an excess CO_2 atmosphere, and the jaws dissected from the animals and defleshed.

To facilitate the assessment of the carious lesions, the jaws were soaked in a Kernechtrot solution (Merck, art. no. 5189), which gave the lesions a red appearance. Enamel caries on buccal plus lingual, proximal, and sulcal areas was scored by one person, in accordance with Keyes (10), as modified by Larson (11), using a blind procedure. By this method the various types of lesions are scored by using estimates of the linear spread and the depth of penetration.

Statistical analysis was done with the Kruskall–Wallis test followed by non-parametric Tukey-type multiple comparisons (12). The level of significance for differences between groups was chosen as $p < 0.05$.

Results

The caries scores for the buccal plus lingual, proximal, and sulcal areas and the total caries score are presented in Table 1. There was a statistically significant ($p < 0.05$) reduction in the caries scores for the buccal plus lingual surfaces, the sulcal areas, and the total caries score for all fluoride groups when compared with the control group, whereas the caries scores for the proximal surfaces in the fluoride groups were not different from those in the control group. Differences between the three fluoride groups were not statistically significant.

Two rats in group 3 died for unknown reasons. The experimental procedures did not significantly affect the average weight gain of the animals.

Discussion

The results showed that topical fluoride treatment with NaF, acidulated NaF, and TiF_4 inhibits carious lesion formation in rats. Evidently, all fluoride treatments had

Table 1. Effect of topical fluoride application on caries scores for different tooth surfaces after 55 days, mean ± SD. Means that are not statistically different ($p < 0.05$) are bracketed by vertical lines

Treatment group	Buccal+lingual surfaces	Proximal surfaces	Sulcal areas	Total caries score
Water, $n=15$	4.3 ± 3.5	4.7 ± 1.5	20.5 ± 6.5	29.5 ± 9.0
NaF, pH 7, $n=15$	0.8 ± 1.1	4.5 ± 2.2	12.1 ± 6.5	17.4 ± 8.6
NaF, pH 1.5, $n=13$	0.9 ± 1.3	3.9 ± 2.6	9.5 ± 6.7	14.3 ± 9.7
TiF_4, pH 1.5, $n=15$	1.0 ± 1.5	2.6 ± 2.9	9.1 ± 6.4	12.7 ± 9.5

significant effect only on the surfaces readily available for the introduced fluoride, whereas proximal surfaces seemed to get no protection from the topical application. This presumably demonstrates that insufficient amounts of fluoride diffuse into the proximal areas.

A tendency to more effective inhibition of decay by acidic fluoride solutions compared with neutral sodium fluoride can be explained by formation of more calcium fluoride on enamel (13–16) and by greater fluoride uptake in the enamel (1, 17), which will exert a caries-inhibitory effect by subsequent release of fluoride ions (15, 16).

A possible difference in the caries-inhibiting effect between TiF_4 and NaF could well be due to differences in pH of the native solutions rather than to the specific metal ions. We therefore thought it important to examine the effect of acidulated NaF with the same pH as the TiF_4 solution. At pH 1.5 and a fluoride concentration of 0.32 M, no significant difference in caries-inhibiting effect between the two compounds was found.

Titanium forms very strong complexes both with fluoride and with enamel (18–20), which may influence the subsequent fluoride release. A strongly retentive Ti-containing surface coating has been observed after treatment of enamel with TiF_4 solutions. The coating is acid-insoluble and not readily removed by washing in artificial saliva or KOH (2, 3, 21, 22). Consequently, this coating may act as a barrier for fluoride release, even in the presence of an acidic environment. On the other hand, the acid-resistant coating may have a protective effect during caries challenge.

The present results are not immediately comparable with those of Regolati et al. (6), who used five daily topical applications of TiF_4 and NaF solutions before a 10-day cariogenic period. After that regimen the caries incidence in the TiF_4 and neutral NaF groups were identical, in spite of higher fluoride content and lower dissolution rate of the TiF_4-treated enamel surfaces. Conceivably, a cariogenic period of 10 days was too short for all fluoride incorporated in the enamel to become reactive. The extended experimental period used in the present study supplements these findings, and, although not statistically significant, a tendency toward lower caries incidence was seen in the TiF_4 group, possibly reflecting greater fluoride deposition by the TiF_4 agent as compared with both neutral and acidified NaF.

It has been shown that fluoride uptake from TiF_4 solutions occurs rapidly. A single application of TiF_4 for 10 sec results in a high fluoride content in root tissue (4). For this reason, TiF_4, in comparison with NaF and varnish treatments, may be more convenient in the clinical situation. As the caries-inhibiting effect of TiF_4 is at least as good as that of NaF, TiF_4 may be the preferred topical prophylactic agent for clinical use.

Acknowledgements.—This study was supported by the Swedish Patent Revenue Research Fund and the Norwegian Council for Science and the Humanities.

References

1. Hals E, Tveit AB, Tötdal B, Isrenn R. Effect of NaF, TiF_4 and APF solutions on root surfaces in vitro, with special reference to uptake of F. Caries Res 1981;15:468–76.
2. Wefel JS, Harless JD. The effect of topical fluoride agents on fluoride uptake and surface morphology. J Dent Res 1981;60:1842–8.
3. Wefel JS. Artificial lesion formation and fluoride uptake after TiF_4 applications. Caries Res 1982; 16:26–33.
4. Skartveit L, Tveit AB, Tötdal B, Selvig KA. Effect of TiF_4 solutions on root surfaces in vitro after different application periods. Acta Odontol Scand 1989;47:25–30.
5. Skartveit L, Tveit AB, Tötdal B, Selvig KA. In vivo uptake and retention of F following a brief application of TiF_4 to dentin. Acta Odontol Scand 1989;47:65–8.
6. Regolati B, Schait A, Schmid R, Mühlemann HR. The effect of titanium, aluminium and fluoride on rat caries. Helv Odontol Acta 1974;18:92–6.
7. Wefel JS, Harless JD. The effect of several topical fluoride agents on artificial lesion formation. J Dent Res 1982;61:1169–71.
8. Reed AJ, Bibby BG. Preliminary report on effect of topical applications of titanium on dental caries. J Dent Res 1976;55:357–8.
9. Keyes PH. Dental caries in the syrian hamster. VIII. The induction of rampant caries actively in albino and golden animals. J Dent Res 1959;38:525–33.
10. Keyes PH. Dental caries in the molar teeth of rats. II. A method for diagnosing and scoring several types of lesions simultaneously. J Dent Res 1958; 37:1088–99.

11. Larson RH. Merits and modifications of scoring rat dental caries by Keyes' method. In: Tanzer JM, ed. Proceedings of a symposium on animal models in cariology. Washington, DC: JRL Press, 1981:195–204.
12. Zar JH. Biostatistical analysis. Englewood Cliffs, NJ: Prentice Hall Inc, 1984.
13. Gerould CH. Electron microscope study of the mechanism of fluoride deposition in teeth. J Dent Res 1945;24:223–33.
14. Saxegaard E, Rölla G. Fluoride acquisition on and in human enamel during topical application in vitro. Scand J Dent Res 1988;96:523–35.
15. Rölla G. On the role of calcium fluoride in the cariostatic mechanism of fluoride. Acta Odontol Scand 1988;46:341–5.
16. Dijkman AG, Arends J. The role of 'CaF_2-like' material in topical fluoridation of enamel in situ. Acta Odontol Scand 1988;46:391–7.
17. Ericsson SY. Cariostatic mechanisms of fluorides: clinical observations. Caries Res 1977;11(suppl 1): 2–41.
18. Clark RJH. The chemistry of titanium and vanadium. New York: Elsevier Publishing Co, 1968.
19. McCann HG. The effect of fluoride complex formation on fluoride uptake and retention in enamel. Arch Oral Biol 1969;14:521–31.
20. Tveit AB, Hals E, Isrenn R, Tötdal B. Highly acid SnF_2 and TiF_4 solutions. Effect on and chemical reaction with root dentin in vitro. Caries Res 1983;17:412–8.
21. Mundorff SA, Little MF, Bibby BG. Enamel dissolution. II. Action of titanium tetrafluoride. J Dent Res 1972;51:1567–71.
22. Wei SHY, Soboroff DM, Wefel JS. Effect of titanium tetrafluoride on human enamel. J Dent Res 1976;55:423–31.

Received for publication 26 January 1990