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Dose Response Effects of Fluoride on Resorption of Deciduous Teeth in Young Rabbits

H.-S. Chen, S.-T. Huang, H.-R. Chen

School of Dentistry, Kaohsiung Medical College, Kaohsiung, Taiwan

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Increasing numbers of reports suggest that fluoride may be of value in the prevention and treatment of some demineralizing bone disorders (Briancon and Meunier 1980; Melton 1990). Fluoride ingestion during tooth formation subsequently results in the formation of dental enamel that better resists caries. However, the major undesired side effect associated with the excessive ingestion of fluoride by children with developing teeth is dental fluorosis (Fejerskov et al. 1977).

In animal experiments, exposure to excess fluoride during tooth development alters tooth morphology (Adkins and Kruger 1966; Kruger 1966), thereby causing cytological modification of ameloblast structure (Kruger 1968, 1970; Walton and Eisenmann 1974; Mornstad and Hammarstrom 1978), diminishes the thickness of enamel and dentine (Adkins and Kruger 1966; Kruger 1966), and induces mineralization disturbances (Fejerskov et al. 1979).

However , the effect of smaller dosages of fluoride on deciduous tooth resorption remains unclear (Chen and Huang 1994). In this study the dose response of fluoride that affects deciduous tooth resorption in vivo is established.

Correspondence to: H.-S. Chen

MATERIALS AND METHODS

16 young, 7-day-old New Zealand white rabbits (Oryctolagus cuniculus) which were in utero for 32 days were used. All root resorption examination in this work occurred during the active stage of the rabbits (Arita 1984).

The animals were divided into four groups. The experimental group (N=12) was divided into three subgroups which were administered intraperitoneal injections of sodium fluoride (Merck, Germany) in dosages of 0.1 mg F/kg body mass, 1.0 mg F/kg body mass or 10mg F/kg body mass in a solution of sodium fluoride twice daily at 8:00 a.m. and 1:00 p.m., respectively. The control group was injected with normal saline solution (0.01 ml/g body mass).

All animals were sacrificed with ether inhalation at the 11th day four hours after the final injection. Immediately after decapitation , the skin and soft tissue were removed. The maxilla of each animal was separated through the palatal suture; in addition both maxillary incisors with the surrounding tissues were fixed in neutral formalin (10%) for 48 h followed by decalcification in Plank-Rychlo's solution for one week. The specimens were embedded in paraffin wax. Furthermore, block sections of the sites were made and treated in accordance with standard histologic procedures. Sections of thickness 7 μm were cut, mounted and stained with hematoxylin and eosin. The specimens were then observed under a light microscope.

The number of odontoclasts were counted according to Saffar and Baron (1977) in each section at intervals of five sections for each animal; hence, the first, sixth, eleventh, and sixteenth sections were examined (at 35 μm intervals). Thus, no attempt was made to follow the same odontoclast; however, our histological criteria for odontoclasts were multinuclear and eosinophyllic cells on the root surface as indicated

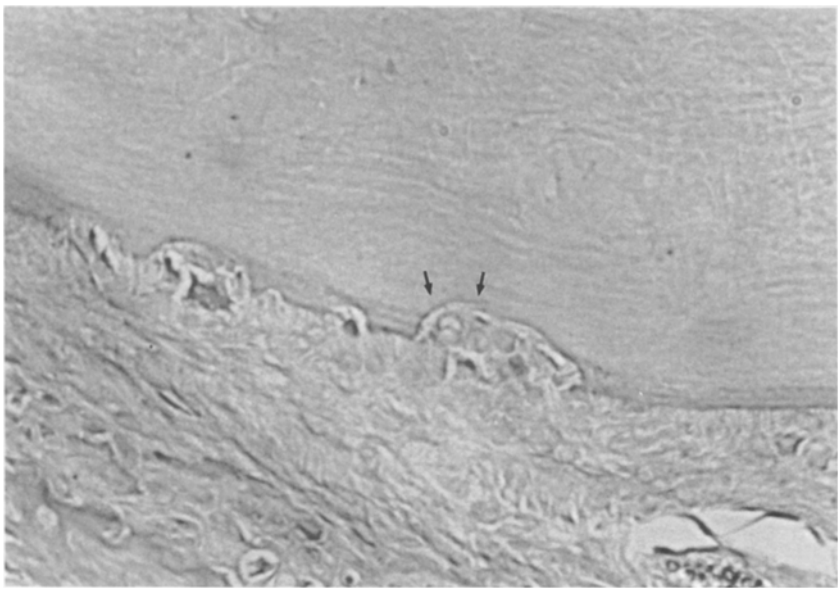

Figure 1. Optical photomicrograph of a deciduous tooth surface, showing a typical odontoclast (arrow) with multinuclear and eosinophyllic cells residing beside the Howship's lacunae (hematoxylin and eosin stain x 200).

in Figure 1. Student's t-test was used to test the level of significance of difference between experimental and control groups.

RESULTS AND DISCUSSION

In this work in which New Zealand young rabbits were used as the animal model, the root resorption of the rabbits resembles that of a human being at both the gross anatomic and ultrastructural levels (Arita 1984). All experimental animals survived the fluoride administration and tolerated the experiment adequately with no apparent discomfort.

Administration of a heavy dose of sodium fluoride (10mg F/kg body mass) markedly inhibited the appearance of odontoclasts ($P<0.001$). Diminished but distinct altera-

tions of odontoclasts were produced by the middle level of fluoride (1.0 mg F/kg body mass) on the 11th day after the injection ($P<0.01$). At the lowest level of fluoride used in this study (0.1 mg F/kg body mass), little or no effect on odontoclasts was apparent. Meanwhile, at high and mild levels (10 and 1.0 mg /kg of NaF), the number of odontoclasts was significantly decreased.

Differences in the mean number of odontoclasts in the control group versus the three experimental groups are listed in Table 1. This table reveals that the odontoclasts were significantly decreased by the administration of fluoride.

Table 1. Comparison of odontoclasts which appear on root surface of deciduous teeth.

	Mean	S.D.	
Control group	54.5	5.2	
		N.S.	
E-1 (0.1 mg F/kg)	51.5	5.5	*
			*
E-2 (1.0 mg F/kg)	37.0	3.6	*
E-3 (10 mg F/kg)	7.2	2.5	

**: $P<0.01$, ***: $P<0.001$
N.S.: not significant

Because root resorption is a physiological phenomenon, the use of saline solution in the control group served to exclude any fluoride-related effect. Administration of sodium fluoride indicated a dose-related inhibitory effect on the appearance of odontoclasts.

The effects of administration of fluoride on mineralizing tissue, e. g. bone, enamel and dentine have been extensively studied (Adkins and Kruger 1966 ; Melton 1990; Kruger 1966, 1968, 1970; Walton and Eisenmann

1974; Mornstad and Hammarstrom 1978). Fluoride intake in large dosages is a well documented cause of disturbed enamel formation during brief experimental period (Kruger 1968, 1970; Walton and Eisenmann 1974; Mornstad and Hammarstrom 1978). Thus, previous knowledge of the minimal effective dose of fluoride during short-term exposure is essential.

In this work, odontoclasts were of primary concern. The odontoclasts are normally found in physiological root resorption, which is the principal cellular mediator of root resorption in deciduous teeth (Ten Cate 1986, Sasaki et al. 1988). Transitory treatment with intraperitoneal injection of fluoride apparently diminishes odontoclastic activity. The resorption of root surface was retarded when the odontoclast number decreased (Chen and Huang 1994). Alterations to this odontoclastic activity and root resorption were produced in graded series and the severity of the alterations apparently depended on the dose of fluoride.

Although serum F levels were not measured in our rabbits, a dosage level of 1.0 mg F/kg, two times per days corresponding to the dose used in humans would most likely lead to serum F concentrations similar to those recorded in treated osteoporotic patients (Briancon and Meunier 1980). In vivo, therapeutic dosages of sodium fluoride are expected to act not only to suppress odontoclastic activity but also to inhibit root resorption.

The dose of 1.0 mg F/kg body mass used in this work is at the borderline level of minimal toxicity for the production of suppressing odontoclast activity. Over the 1.0 mg F/kg of body mass dose used in this study, there was a decreased alteration of the odontoclasts in a graded series. Experimental results indicated that 1.0 mg F/kg of body mass would be a dose response condition such that it creates intake during the critical period of root resorption and would result in further retardation.

As to the mode of action of fluoride in inhibiting odontoclast activity, we recommend, for children, the use of a small concentration of fluoride in the prevention of bone diseases in order to reduce the toxic effect of fluoride to a minimum. This work may provide useful information to those who have been evaluating the causes of idiopathic root resorption.

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