Development of phenytoin-induced gingival overgrowth in non-institutionalized epileptic children subjected to different plaque control programs

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The periodontal condition was studied in phenytoin (PHT)-treated non-institutionalized epileptic children ($n = 59$) subjected to different preventive programs. One group followed an intensive preventive program during a 2-year period initiated before the start of PHT medication. The second group was given a moderate preventive program initiated after various periods of PHT medication. Patients not subjected to any additional preventive program during their PHT medication were used as controls. None of the individuals following the intensive preventive program developed pseudopockets. About 46% of the children in the moderate preventive group and 40% of the individuals not subjected to any preventive program developed pseudopockets. The amount of time the children were without plaque control was significantly and positively correlated to the development of gingival overgrowth. To minimize this occurrence, PHT-treated children should be subjected to a preventive program initiated before the start of PHT medication. □ *Epilepsy; pedodontics; periodontology*

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Gingival overgrowth is a well-known side effect affecting children receiving phenytoin (PHT) medication for the treatment of epileptic seizures (1–4).

Several authors have shown that PHT-induced gingival overgrowth is associated with plaque accumulation and gingival inflammation, but the pathogenesis has still not been established (3–9). According to Pihlstrom et al. (10), gingival enlargement develops within the first 6 months of PHT therapy. We recently studied the effect of a plaque control program initiated before the start of PHT medication (4). The development of PHT-induced gingival overgrowth in epileptic children during a 2-year period was studied. We concluded that none of the patients developed pockets with a probing depth greater than 4 mm, whereas an increased thickness of the marginal gingiva buccolingually was noted in all patients during the observation period.

There is a lack of information concerning the effectiveness of different preventive programs given to outpatients receiving PHT medication. The present investigation was thus undertaken to evaluate the periodontal condition in a group of non-institutionalized epileptic children subjected to different preventive programs during PHT medication. Since the development of the lesion occurs within a few months after start of PHT therapy, we felt that a feasible approach would be to evaluate the influence of the time interval between the start of PHT therapy and inclusion in the plaque control program.

Materials and methods

The children included in the study ($n = 59$) were being treated for different types of epilepsy at the Department of Pediatrics, Huddinge University Hospital. The pharmacotherapy used is presented in Table 1. The children were subdivided into three groups:

Table 1. Pharmacologic treatment of the patients

Drugs	No prevention (n = 30)	Moderate prevention (n = 13)	Intensive prevention (n = 16)
Phenytoin (Fenantoin®) (F)	25	9	16
F + carbamazepine (Tegretol®)	1	2	—
F + sodium valproate (Orifilept®)	1	2	—
F + primidone (Mylepsin®)	1	—	—
F + clonazepam (Iktoviril®)	1	—	—
F + ethosuximide (Suxinutin®)	1	—	—

Intensive preventive program

Children (n = 16) belonging to this group have previously been described by us (4) and comprised 7 boys and 9 girls with a mean age of 11.1 years. The children had been receiving PHT medication for an average of 2.0 years. A specific preventive program was initiated before the start of PHT medication and included information to the patients and parents concerning the oral side effects of PHT medication, instruction in the Bass tooth-brushing technique, and instruction in the use of dental floss for patients with a permanent dentition. Professional tooth-cleaning was performed at each visit.

The subjects were recalled once a week during the 1st month and after 1.5, 3, 4, 5, 6, 9, 12, 15, 18, 21, and 24 months of PHT therapy.

Moderate preventive program

Children (n = 13) belonging to this group consisted of 6 boys and 7 girls with a mean age of 11.8 years and had received PHT medication for approximately 4.5 years. The children did not have any regular preventive program at the start of PHT therapy. The children were referred by their physicians to the Department of Pedodontics for preventive therapy at various times after the initiation of PHT medication. The mean time was 2.8 years, with a range of 0.1 to 8 years. All the children were given information, motivation, and instructions similar to those given the children taking part in the intensive preventive program. Professional tooth-cleaning was performed every 3rd month for an average of 24 months.

No preventive program

These children (n = 30) have earlier been described (4) and consisted of 13 girls and 17 boys with a mean age of 13.2 years. They had been receiving PHT medication, sometimes in combination with other anti-epileptic drugs, for an average of 5.5 years and were not subjected to any additional plaque control program other than the prophylaxis given in connection with the annual treatment provided by the Public Dental Service.

Clinical assessment

Oral hygiene status was assessed by means of the visible plaque index (VPI) (11). The presence of dental plaque was revealed by using a disclosing agent on the four surfaces of all available teeth. The VPI percentage was expressed as the number of surfaces showing plaque divided by the total number of surfaces available.

Gingival condition

Gingival inflammation was estimated by the gingival bleeding index (GBI) (11). Individual percentages of surfaces with gingivitis were based on the occurrence of bleeding on probing the gingival sulcus.

Gingival overgrowth

Sulcus depth was measured proximally to the nearest millimeter, using a graded periodontal probe. Surfaces with increased pocket (pseudopockets) depth (>4 mm) were recorded. Gingival overgrowth was also determined on stone casts on the basis

of the thickness of the marginal gingiva buccolingually. Measurements were made in the incisor region, in the maxilla and the mandible. The thickness of the marginal gingiva was measured from the buccal surface of the tooth to the most prominent point on the marginal gingiva, as previously described by us (4). The relative space in both arches was also determined on the stone casts (12).

The serum level of PHT was estimated by fluorescence polarization immunoassay (TDX, Abbott) (13).

Statistical analysis

A non-parametric statistical method, the Mann–Whitney U-test, was used to test the significance of differences between groups. Pearson's correlation test was also used for inter-parameter relationships with regard to the moderate preventive group.

Results

The mean values and standard deviations of the variables in the three groups are presented in Table 2. The children following the intensive preventive program showed a significantly ($p < 0.05$) lower frequency of surfaces with plaque compared with individuals not subjected to any preventive program. No inter-group differences were found with regard to the mean frequency of units with gingival bleeding. Compared with the children in the intensive prevention group, gingival overgrowth, on the basis of the occurrence of pseudopockets, was significantly more frequent among the children in the moderate preventive group ($p < 0.01$) and those not subjected to any preventive measures ($p < 0.001$). There was, however, no difference in the frequency of pseudopockets between the children following the moderate preventive program and those not receiving any prophylaxis during PHT medication.

Gingival overgrowth buccolingually in the mandibular incisor region differed significantly for the three groups. In the maxilla the only significant difference obtained was between the children in the intensive pre-

Table 2. Mean values ($\bar{x}$) and standard deviations (SD) of the variables examined

Variables	No prevention		Moderate prevention		Intensive prevention		Significance		
	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	No versus moderate	No versus intensive	Moderate versus intensive
GBI, %	15.1	11.0	14.5	6.1	13.6	7.9			
VPI, %	42.8	11.0	35.9	17.0	30.7	14.1		*	
Patients with increased probing depth (>4mm), no.	12		6		0			**	***
Gingival thickness buccolingually									
Maximillary incisor	1.4	0.40	1.3	0.39	1.1	0.24		*	
Mandibular incisor	1.5	0.54	1.1	0.30	0.9	0.27	**	***	**
Serum conc. of PHT (μmol/l)	55.7	18.6	43.2	16.3	48.8	17.7			

* = $p < 0.05$; ** $p < 0.01$; and *** $p < 0.001$.

Table 3. Pearson product moment correlation test of variables in PHT-treated children following the moderate preventive program

	Gingival overgrowth	
	Thickness of marginal gingiva	Increased probing depth (>4mm)
Age	0.017	0.321
Years of PHT therapy	0.611*	0.684**
GBI, %	0.064	0.392
VPI, %	−0.301	−0.111
Probing depth (>4mm)	0.795**	—
Thickness of marginal gingiva	—	0.795**
Time without plaque control program	0.592*	0.718**
Relative jaw space	0.734**	0.576*
Serum conc. of PHT	0.277	0.291

* = $p < 0.05$; ** = $p < 0.01$.

ventive group and individuals not subjected to any prevention.

To study the influence of the time interval between the start of PHT medication and initiation of the preventive program, interparameter correlations were tested in the moderate preventive group (Table 3). No statistically significant correlation was found between the plasma level of PHT and gingival overgrowth. On the other hand, 'years of PHT therapy' and 'relative jaw space', 'thickness of marginal gingiva', and the time interval between the start of PHT therapy and initiation of the preventive program were all positively correlated to the occurrence of gingival overgrowth.

Discussion

The effect of different plaque control programs on the development of PHT-induced gingival overgrowth was studied in 59 epileptic children. The plaque score of patients not subjected to any prevention was in accordance with that reported by Lundström et al. (14), who studied PHT-treated epileptics of a similar age. In contrast to the level of gingivitis, the plaque level was significantly lower among the children following the intensive preventive program compared with patients not subjected to any special prevention. All the children did, however, receive dental prophylaxis in connection with their annual check-up provided by the Public Dental Service.

In this study no correlation between gingival overgrowth and gingivitis was found among the children following the moderate preventive program. This is in contrast to the findings of Aas (15), Angelopoulos & Goaz (16), Hassell et al. (17), and King et al. (8) but in agreement with those of Klar (1) and Modéer et al. (3). The fact that PHT-treated children not subjected to any prevention had significantly higher plaque levels but similar gingivitis scores compared with the children following the intensive preventive program is interesting in view of the results of Gupta et al. (18). They found that PHT had an anti-inflammatory effect interacting with glucocorticoid receptors, resulting in the inhibition of prostaglandin, thromboxane, and/or leukotriene production. Furthermore, adults receiving long-term PHT medication have significantly less alveolar bone loss than those receiving sodium valproate therapy (19).

No correlation was found between the serum levels of PHT and gingival overgrowth. This is in agreement with the findings of most authors (14, 16). When gingival overgrowth was based on the occurrence of pseudopockets, none of the individuals following the intensive preventive program had developed pseudopockets, compared with 46% of the children in the moderate preventive group and 40% of the individuals not

subjected to any additional prevention. Gingival overgrowth was also characterized in the buccolingual dimension with an objective method whereby the most prominent point on the marginal gingiva of the maxillary and mandibular incisors was measured on stone casts (4). Significant group differences in buccolingual thickness were noted in the mandible. In the maxilla, however, only children in the intensive preventive group differed significantly with regard to the thickness of the marginal gingiva. When comparing the influence on gingival overgrowth of the different preventive programs used in our study, one must consider that the period of medication varied for the groups. This variation may be of importance, since there was a significantly positive correlation between years of PHT therapy and development of gingival overgrowth in children following the moderate preventive program.

To increase the effectiveness of prevention against PHT-induced gingival overgrowth, the results of this study indicate that plaque control must be initiated before the start of PHT therapy. This was supported by the fact that the time interval between the start of PHT medication and initiation of the preventive program was positively correlated to the occurrence of gingival overgrowth. This assumption is also supported by the fact that development of gingival overgrowth seems to occur within 6 to 9 months of initiation of PHT therapy (4, 10). In our opinion, plaque control must be performed in close cooperation with the pediatrician responsible for the medical care of the child.

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