MARIA MIELNIK-BŁASZCZAK, AGNIESZKA SKAWIŃSKA, ARTUR MICHAŁOWSKI,
JERZY BŁASZCZAK, KATARZYNA KSIĄŻEK

The impact of antiepileptic drugs on the condition of the oral cavity in children and youth affected with epilepsy

Abstract

Introduction. Epilepsy is one of the most common neurological disorders. Epileptic patients taking antiepileptic pharmaceuticals often suffer from hypertrophic changes in gums. It is well established that dental hypertrophies within the alveolar tissue appear more often in children and young people being treated for epilepsy than adults.

Aim. The aim of the study was to determine the influence of antiepileptic drug therapy on the oral cavity of both children and young people suffering from epilepsy.

Material and methods. The investigation consisted of a clinical examination and a questionnaire looking at 107 individuals of both sexes, all aged between 6 and 18. They were all residents of the Lublin region. The study looked at the individuals residing in the Social Care Center in Lublin and patients treated at the Children's Clinical Hospital in Lublin. The oral analysis included an examination of hard tissues, the state of oral hygiene according to Green and Vermillion (OHI-S), periodontal treatment needs (CPITN), status of gums and mucosal membrane pathological assessment of the oral cavity and determination of developmental disturbances of teeth (intensity of tooth decay expressed as DMFt).

Results. The patients who took antiepileptic drugs had greater treatment needs in tissues of periodontium – determined by the value of CPITN index – (1.68 ± 0.60), unlike those subjects who had not taken any medicine (0.96 ± 0.29), ($p=0.0001$; $Z=-3.20$). It was stated that the value of the DMFt index had been significantly higher in those subjects who had been taking antiepileptic medicines (6.80 ± 5.16), unlike the subjects not taking medicine (4.65 ± 3.72), ($p=0.02$; $Z=2.40$). In subjects taking antiepileptic drugs, the OHI-S index was significantly higher (2.50) unlike those subjects who had not taken any medicine (1.53), ($p=0.0001$; $Z=4.92$).

Conclusions. The findings demonstrate that the hard dental tissues in children taking antiepileptic drugs require much more care. They have a higher simplified index of oral hygiene and higher index for periodontal treatment needs. Disturbances related to oral mucosal cavity and dental abnormalities occurred more frequently in children ingesting antiepileptic agents.

Keywords: children, youth, CPITN, OHI-S, antiepileptic drugs.

DOI: 10.1515/pjph-2015-0035

INTRODUCTION

Epileptic patients taking antiepileptic pharmaceuticals often suffer from hypertrophic changes in gums [1]. Hypertrophic changes were observed after a 3-months long therapy made on 50% patients receiving phenytoin [1]. Similar adverse effects occurred following the administration of other anticonvulsants, such as valproic acid or carbamazepine [2]. The exact cause of the drug – induced gingival enlargement has yet to be discovered but there is a number of hypotheses [3].

According to various researchers, hypertrophy starts in the interdental papilla, and then proceeds to the alveolar gingiva [2]. Later, some pale rosy gingival flaps with a floppy structure start to appear, covering the entire crowns. In the frontal area of dental arches, hypertrophic symptoms appear with greater intensity and the changes that happen make it difficult to maintain proper hygiene standards, which leads to

the development of inflammatory conditions. The presence of gingival hypertrophy subsequently supports the accumulation of dental plaque and produces difficulties with respect to hygiene, leading to development of caries diseases, triggering recurring infections, and bleeding of gums. Recurrent secondary infections make the gum inflammation even more severe, later developing into periodontitis, which is fibrous in nature [1,4]. It is well-established that dental hypertrophies within the alveolar tissue appear more often in children and young people being treated for epilepsy than adults [2]. However, no pathological mechanisms caused by the antiepileptic drug-induced oral hypertrophies have been found but it was suggested that bacterial plaque may be involved [2]. Other factors contributing to drug-induced hypertrophic changes include a decrease in levels of folic acid [1], an increased concentration in biologically active androgens [1] and reduction in IgA levels in alveolar tissue [2].

Patients who received either valproic acid or carbamazepine tend to develop dental hypertrophies, although the incidence is less severe in 25% patients [1].

Salivary hyposalivation is another adverse effect caused by the use of antiepileptic therapeutic agents. It may cause a significant fall of pH, even below the critical level of 5.5 at which point there is a destruction of the enamel [5]. In patients suffering from epilepsy, antiepileptic drug-induced salivary hyposalivation is a disease characteristic classified as type I genuine xerostomia with characteristic features, such as dryness in the oral cavity, difficulty in swallowing, burning lips and/or the tongue, taste disorders, and acute tooth decay. During periods of reduced resistance, dryness of the oral cavity supports superinfection with yeast fungi (*Candida albicans*) [6].

AIM

The aim of this study was to determine the influence of antiepileptic drugs on the oral cavity of children and young adults with epilepsy being treated with antiepileptic drugs in Lublin, Poland.

MATERIAL AND METHODS

The research included both a clinical examination and a questionnaire examining 107 children and youth of both sexes. The age ranged from 6 to 18 and all the participants were residents of the Lublin region, including individuals appointed to the Social Care Center in Lublin and patients treated at the Children's Clinical Hospital in Lublin. Amongst the examined patients 56%, (n=60) were boys and 44%, (n=47) girls (Table 1). Some 71% of the investigated children took antiepileptic drugs, whilst 29% of children were not subject to any drug regimes. The oral analysis included an examination of hard tissues, the state of oral hygiene according to Green and Vermillion (OHI-S), periodontal treatment needs (CPITN), condition of gums and mucosal membrane pathological assessment of the oral cavity and determination of developmental disturbances of teeth (intensity of tooth decay expressed as DMFT). Both the control group and the patient group were subjected to a clinical examination. The children and young adults were examined for a period of approximately 1 year during which they received antiepileptic agents. The control group consisted of 36 patients.

A statistical analysis of the data was performed.

Results were expressed as mean and standard deviation and for non-measurable values cardinality and % were used. For measurable features, the normalcy of the disintegration of analyzed parameters was assessed with the help of Shapiro-Wilk test.

For comparing two independent groups, Mann-Whitney test was applied, and for more than two groups Kruskal-Wallis was applied. A $p < 0.05$ significance level was set as the criterion for significance. Database and statistical evaluation was conducted using STATISTICA 8.0 (StatSoft, Polska) software.

TABLE 1. Patient characteristics.

Parameter	Control	Epileptic group
Age		
6-12	17	35
12-18	19	36
Gender		
M	21	39
F	15	32
Drugs		
Valproic acid,	0	42
Carbamazepine	0	29

TABLE 2. Occurrence of gingiva and oral mucosa alterations caused by antiepileptic drugs.

	Gingiva and oral mucosa alterations	No changes	Total	Statistical analysis
	n %	n %	n %	
Yes	56	15	71	Chi ² =18.63 p=0.00002*
	78.9%	21.1%	100%	
No	13	23	36	
	36%	64%	100%	

FIGURE 1. CPITN value.

FIGURE 2. OHI-S index.

RESULTS

The statistical analysis shows that the patients who took antiepileptic medicines had greater treatment needs in tissues of parodontium – determined by value of a CPITN index – (1.68 ± 0.60) unlike those subjects who had not taken any medicine (0.96 ± 0.29), ($p=0.0001$; $Z=-3.20$). Such value of CPITN is a reason for gum bleeding, the calculus felt during probing and, in the rare cases, it causes periodontal pockets 4 or 5 mm depth to appear. (Figure 1). Examinations showed that the changes associated with the mucous membrane of the oral cavity of inflammatory and hypertrophic changes were more likely to appear in children and young people taking antiepileptic medicines (78.9%) compared with those who didn't take medicines (36%), ($p=0.00002$; $\chi^2=18.63$).

It was stated that the value of the DMFT index had been significantly higher amongst those subjects who took antiepileptic medicines (6.80 ± 5.16) compared with the subjects not taking medicines (4.65 ± 3.72), ($p=0.02$; $Z=2.40$). Those subjects who took antiepileptic medicines had the significantly higher D number (4.36 ± 4.15) compared with the subjects who didn't take medicines (1.90 ± 1.47), ($p=0.003$; $Z=3.02$). The value of the DMFT index shows the intensity of the dental caries, in this case it is significantly higher.

An analysis showed that in subjects taking antiepileptic medicines OHI-S index was significantly higher (2.50) compared with those subjects who didn't take medicines (1.53), ($p=0.0001$; $Z=4.92$). The value shows that the soft debris and dental calculus covers more than one third of the exposed tooth surface. (Figure 2). Important differences also appeared in its components. DI-S index in subjects taking antiepileptic medicines amounted to 1.94 ± 0.66 , and of those subjects who didn't take medicines it reached 1.43 ± 0.67 , ($p=0.00007$; $Z=-3.39$). Highly significant differences were stated in the value of an CI-S index – in subjects taking antiepileptic medicines, it amounted to 0.56 ± 0.55 , and in the group of subjects who didn't take medicines it was 0.10 ± 0.18 ($p=0.000001$; $Z=-4.60$).

DISCUSSION

There are some authors that discuss the relationship between taking antiepileptic medicines and the etiology of hypertrophic gum changes, along with the impact of dental hygiene. Antiepileptic medicines modify the response of the tissue to the inflammatory factor which is expressed in the clinical picture of the parodontium and presence of exponents of inflammation [7]. The changes happening during the treatment are mainly of hypertrophic character. However, what causes them is yet to be discovered. The treatment of the lesions in the parodontium is difficult, as it is sometimes impossible to replace the current medicine with another, without causing some undesired side effects (e.g. in epilepsy) [2]. The percentage given by authors of subjects in whom hypertrophic changes appeared differs significantly.

The authors of this study can confirm that bad hygiene can lead to hypertrophic changes within the parodontium. It may also cause an occurrence of illness of hard dental

tissues. For example, the authors conducted studies that show that the mean values of DMFT number were significantly higher amongst the subjects who took antiepileptic medicine (6.80 ± 5.16), unlike compared with the subjects not taking medicines (4.65 ± 3.72), ($p=0.02$; $Z=2.40$). The subjects that took antiepileptic medicines had significantly higher OHI-S index (2.50), unlike the subjects not taking medicine (1.53), ($p=0.0001$; $Z=4.92$). In the study by Gurbuz, who looked at epileptic patients, achieved a lower DMFT number value (3.5 ± 3.79) [8].

Patients treated for epilepsy should pay special attention to care of their oral cavity. Various therapeutic aspects of treating epilepsy have been researched by numerous scientists for years. Antiepileptic medicines exerting a direct effect on functioning of the organism should be appropriately selected and applied in doses allowing minimizing the occurrence of adverse side effects. Monitored epilepsy treatment is raising new hopes. Its purpose is a control of the concentration of medicines in bodily fluids leading to setting optimum doses for each suffering individual [9].

CONCLUSIONS

1. Using antiepileptic medicines in children or young people treated for chronic epilepsy might cause hypertrophic changes in the alveolar tissue.
2. Increased rates in the DMFT Index, and of its component – D Index confirm that the therapy affects the condition of hard tissues of teeth.
3. Condition of the dental hygiene is unsatisfactory in children treated for epilepsy.

REFERENCES

1. Panek H, Sobolewska A, Kleczyk M, et al. Pacjent z epilepsją w gabinecie stomatologicznym. *Protetyka Stomatol.* 2007;57:171-5.
2. Borowicz-Andrzejewska E. Periodontal condition and level of oral hygiene in children treated with carbamazepine and valproic acid. *Czas Stomatol.* 1999;50:576-81.
3. Lin K, Guilhoto L, TargasYacubian E. Drug – induced Gingival Enlargement. Part II. Antiepileptic drugs: Not only phenytoin is involved. *J Epilepsy Clin Neurophysiol.* 2007;13:83-8.
4. Prasad VN, Chawla HS, Goyal A, et al. Incidence of phenytoin induced gingival overgrowth in epileptic children: a six month evaluation. *J Indian Soc Pedod Prev Dent.* 2000;20:73-80.
5. Szpringer-Nodzak M, Wochna-Sobańska M. *Stomatologia wieku rozwojowego.* Warszawa: PZWL; 2006. p. 251-73.
6. Karolyhazy K, Kivovics P, Fejerdy P, Aranyi Z. Prosthodontic status and recommended care of patients with epilepsy. *Prosthet Dent.* 2005;93:177-82.
7. Borowicz-Andrzejewska E. The occurrence of gingival hyperplasia in children treated for epilepsy with carbamazepine and valproic acid. *Epilepsia.* 1996;37:694-7.
8. Gurbuz T. Oral health status in epileptic children. *Pediatr Int.* 2010;52:279-83.
9. D'Souza W, O'Brien TJ, Murphy M, et al. Toothbrushing-induced epilepsy with structural lesions in the primary somatosensory area. *Neurol.* 2007;68:769-71.

Corresponding author

Agnieszka Skawińska
7 Karmelicka Str., 20-081 Lublin
E-mail: Agnieszka.Skawinska@gmail.com