Five-year follow-up of oral health and seizure condition of patients with epilepsy: a prospective observational study

Katalin Károlyházy[1], Péter Kivovics[1], Péter Hermann[1], Pál Fejérdy[1], Zsuzsanna Arányi[2]

[1]Dept. of Prosthetic Dentistry, Faculty of Dentistry, Semmelweis University, Budapest, Hungary

[2]Dept. of Neurology, Faculty of Medicine, Semmelweis University, Budapest, Hungary

Corresponding author: Zsuzsanna Arányi MD, PhD

Dept. of Neurology, Faculty of Medicine, Semmelweis University

Balassa u. 6.

Budapest, Hungary- 1083

Telephone: (+36-1)-210-0330

Fax: (+36-1)-210-1368

E-mail: zsuzsi@neur.sote.hu

Key words: epilepsy, oral health, periodontal state

Word count of main text: 2594

Abstract

Objective: A five-year follow up of patients of epilepsy to examine the change in their oral health and seizure condition.

Basic research design: A prospective observational controlled epidemiologic study under naturalistic treatment settings.

Participants: The epilepsy group consisted wholly of patients participating in an epidemiologic survey performed 5 years previously. The gender- and age-matched control (none-epilepsy) group consisted partly of subjects recovered from the previous study, and partlyof new subjects.

Interventions: Data pertaining to the disease were collected and a thorough dental examination was performed.

Main outcome measures: Indexes quantifying oral hygiene, the number and condition of the remaining teeth, periodontium, and the degree of prosthetic treatment were measured. Statistical comparison was performed between the patient and the control group of the present study, and pair wise between the previous and the present survey.

Results: The epileptic condition of the patients showed significant improvement upon follow-up, in contrast to a significant deterioration in their oral health as compared to the control group. Concerning oral health, dental indices describing oral hygiene and periodontal condition showed the most pronounced decline.

Conclusions: The improvement in the epileptic condition of patients is attributed to changes in treatment strategies. As the epileptic condition and oral health of patients changed in opposite directions, socioeconomic and educational factors appear to play a more important role in the poor oral health of these patients than disease-specific factors (e.g. oral cavity injuries, increased exertion on the teeth, antiepileptic drug effects). Furthermore, the periodontal condition seems to be main factor responsible for the unfavourable dental status.

Introduction

Patients with epilepsy may be negatively affected by their condition in many ways that are not necessarily a direct consequence of their seizures. One such example is an adverse effect on oral health and dental status, which is an important aspect of quality of life, from both medical and social point of view (Westphal 1972, Friedlander and Cummings 1989, Ogunbodede et al. 1998, Shaw et al. 1990, Dahllöf et al. 1993). We have previously conducted for the first time a controlled dental and neurological epidemiologic survey on a consecutive series of patients with epilepsy and found that in almost all aspects of oral health and dental status (i.e., the state of remaining teeth and periodontium, extent of restorative and prosthetic treatment), patients with epilepsy showed a significantly worse condition compared with an age-matched group of general (none-epilepsy) population (Károlyházy et al, 2003). Furthermore, patients with poorly controlled epilepsy exhibited the worst oral health. These findings were explained by the combined effect of seizures, the socioeconomic background of patients, and the negative attitude of dentists. The well known gingival effect of phenytoin (Dahllöf et al. 1993) was not an issue in our sample, as very few patients were taking the drug. To facilitate and encourage individualized dental care of these patients, we have also set up a unique 'dental' classification of epilepsy patients, based on the type and frequency of seizures and their possible effect on the masticatory apparatus, and patient compliance; we have also given specific recommendations for dental care for each group (*Table 1*) (Károlyházy et al. 2003, Károlyházy et al. 2005).

With the aim to assess the change in dental status and oral health of the group of patients participating in the above mentioned survey, we have followed them up five years after the original survey. An effort was made to recover the same control group as well. In addition to this 'dental' information, we were also curious to see how the seizure condition has changed of this non-selected, general population of patients with epilepsy in the era when pharmacological treatment of epilepsy is undergoing a fundamental change.

Patients and Methods

The study was performed as a collaboration of the Department of Prosthetic Dentistry, Faculty of Dentistry, and the Department of Neurology, Faculty of Medicine, of the Semmelweis University in Budapest five years after the first survey (2001-2002). All patients and control subjects gave informed consent. Patients enrolled into the study are the patients under the regular care of the epilepsy outpatient unit of the Department of Neurology, a secondary referral centre for epilepsy. Of the 101 patients examined in the first survey, 71 were recovered: 22 were lost to follow-up (most of them moved away from the area), 4 refused examination and 4 had died (2 due to stroke, 1 to myocardial infarct, 1 to brain tumour). Of the 101 control subjects of the first survey, 35 were recovered; 36 new control subjects were added, gender and age-matched to the epileptic population. Data were collected by the same two investigators as in the first study (neurologist- Zs.A., dentist- K.K.).

First, personal information and data pertaining to the change of epileptic condition of the patients were recorded by the neurologist in a numeric form, suitable for statistical analysis. These included change of seizure frequency and type, any oral injuries occurring in the five-year interval, change of antiepileptic drugs (AED), present AEDs and their doses. The patients were then reclassified by the neurologist according to their present condition and were put in the appropriate dental subgroup, as defined previously (*Table 1*) (Károlyházy et al. 2003).

A dental examination then followed, which was performed under standard conditions in exactly the same way as during the first study. For detailed description of the measurement of the dental indices, please refer to the original publication (Károlyházy et al. 2003). In summary, criteria used for the diagnosis of oral disease were consistent with those recommended by the World Health Organization (WHO 1997). Similar to the neurological questionnaires, all the data collected during the dental examination were recorded in numeric form on a prepared sheet. The examination included the following: *dental history*, assessment of *oral hygiene* (Greene-

Vermillon Oral Hygiene Index), *remaining teeth* (determination of the number of decayed, missing and filled teeth [DMF-T Index]), degree of tooth *abrasion* (categorized as superficial or deep separately for upper and lower teeth; expressed as percentage of patients exhibiting abrasion), *periodontal status* (Community Periodontal Index of Treatment Needs [CPITN] Index, periodontal attachment loss, Mühlemann Index of gingival bleeding), *prosthetic appliances* and the ratio of artificial and missing teeth (Prosthetic Index), and *stomatooncological examination*. Control subjects underwent an identical dental examination.

Statistical analysis was performed by the same statistician as in the previous study, using the SAS v. 9.1.3 STAT program. Comparisons were performed between the epilepsy and the control group of the present study and between three dental subgroups of epilepsy patients of the present study. Furthermore, the epilepsy group of the previous and present study and the control group of the previous and present study (in this case only those 35 control subjects were included who participated in both surveys) were pair wise compared to each other, to look for any change upon follow-up. Group means and standard deviations were calculated using SAS BASE MEANS FREQ procedures. The Wilcoxon test was used for age comparisons. Comparison of abrasion was done by the $\chi 2$ statistic. All the other indexes describing oral health (Greene-Vermillon Oral Hygiene Index, DMF-T Index, etc.) were analysed by using the SAS General Linear Model (modified two-tailed *t* test). In the follow-up comparisons, the Friedmann's repeated measures of $\chi 2$ statistic were used for discrete variables, and the ANOVA model for continuous variables. To compare the degree of change between the epilepsy and the control group, the General Linear Model (modified two-tailed *t* test) was used. Statistical significance was set at $p < 0.05$.

Results

The average age of the patient and control group was not significantly different ($p = 0.6$). The average time of follow-up was 5 years and 4 months ± 4 months for the epilepsy group, and 4 years and 8 months ± 1 month for the control group.

There was a significant improvement with respect to the dental classification of the epilepsy patients ($p=0.0126$). *Figure 1* shows the favourable change in the proportion of patients in Groups I-III during the first and the follow-up study. Altogether 11 patients moved from high risk groups to lower risk groups. The direction of change was negative for only 2 patients, but it was a minor deterioration (moving from Group I to II). In association with this improvement, the frequency of generalised tonic-clonic seizures was significantly reduced ($p=0.001$) during the five-year interval. A similar tendency was observed for other seizure types as well, however it did not reach significance.

The percentage of active (employed) workers decreased by 10% in the epilepsy group and increased by 8% in the control group ($p<0.0001$).

Concerning the AEDs, a significant decrease (from 39.4% to 29.6%) was seen in the percentage of patients taking carbamazepine ($p=0.0348$), and a significant increase (from 19.7% to 29.6%) in the percentage of patients taking lamotrigine ($p=0.0348$). Carbamazepine was taken in combination with other AED(s) by about half of the patients, whereas lamotrigine was combined in two-thirds of the patients. Valproate remained a strong hold medication with 49.3% and 47.9% of patients taking it in the previous study and the present study, respectively. Valproate was taken in combination with other AEDs by two-thirds of the patients. Percentages of patients taking other AEDs in the present study: levetiracetam (5%), topiramate (4.2%), oxcarbazepine (5.6%), phenytoin (1%), primidone (5.6%), phenobarbital (1.4%), gabapentin (2.8%), clobasam (11.3%), clonasepam (4.2%). Of these drugs, levetiracetam, topiramate, and oxcarbazepine were newly introduced.

The results of the dental indices are presented in *Table 2*. Group mean values with standard deviations are given only for the present study; significance levels are shown for comparisons between the epilepsy and the control group of the present study, between the epilepsy group of the present and previous study (followed-up patients), and between the control group of the present and previous study (including only the followed-up control subjects). The extent of change in the two groups upon follow-up was also compared.

In summary, the Greene-Vermillon Oral Hygiene Index (OHI-S) assessing oral hygiene was significantly worse in the epilepsy group in the present study; in the previous study this difference did not reach significance. This is reflected in the significant increase of the OHI-S index within the epilepsy group when comparing the values of the previous and the present study. The opposite change was observed in the control group. In other words, oral hygiene has deteriorated in epilepsy patients, and improved in control subjects. The DMF-T index, a complex index assessing the remaining teeth, was again significantly higher in the epilepsy group, just as in the previous study. During the follow-up there was a significant increase in both groups, but the extent of change was not significantly different between the epilepsy and the control group. Concerning abrasion, it was significantly more pronounced in patients with epilepsy; in the previous study this difference was seen only in poorly controlled patients (Group III), upon follow-up the difference reached significance for the whole group. However also in the follow-up study, abrasion for the lower teeth was most pronounced in Group III (comparison between Group II and III: $p=0.0004$). The degree of progression of abrasion was similar in patients with epilepsy and control subjects. The periodontal status is characterised by the CPITN index, the periodontal attachment loss (PAL), and the Mühlemann index of gingival bleeding. It is seen in *Table 2* that for all three indices patients with epilepsy exhibited a significantly worse condition in comparison to control subjects; both groups have shown progression, but it is significantly more pronounced in epilepsy patients. *Figure 2* shows the increase in periodontal attachment loss as compared to the previous study. This increase is

significantly higher in the epilepsy group. Gingival hypertrophy was again not seen, even in the one patient still on phenytoin therapy. Finally, the prosthetic index -indicating the extent of restorative-prosthetic treatment – was again significantly lower (i.e. less favourable) in patients with epilepsy. The change was not significant in either group.

Discussion

Of the 101 patients participating in the original survey 5 years previously, 71 patients were recovered and underwent an identical neurological and dental assessment. In fact, all of these patients remained under the care of the examining neurologist. These patients were first compared as a group to a control group that consisted of about half of the original control subjects (the other half being new), and then pair wise compared to their own first assessment. A similar comparison was done for the control group as well, however this time only including those subjects who have participated in both surveys.

It was shown that the epileptic condition of the patients had improved significantly, as indicated by the reduction of generalized tonic-clonic seizures and the favourable change in the distribution of patients in our dental classification (*Fig. 1*). The proportion of patients in Group I (including mostly seizure-free individuals) increased and reached almost 75%, with the simultaneous decrease of the proportion of patients in the poorly controlled groups (mainly Group III). Altogether 10% of the original patient sample showed improvement in seizure condition. This positive change in the seizure condition of these patients doesn't appear to be the result of an improvement in patient compliance, which remained fairly constant throughout the period of 1997-2008 in this epilepsy out-patient unit observed by the same physician (Zs.A.). The favourable change in the seizure condition of patients is attributed to the introduction and increased use of second generation AEDs and a change in treatment strategies. The results of our study contribute to the demonstration of the overall benefit of new AEDs a group, under naturalistic treatment settings in a general epilepsy population.

With regard to the results of the dental examination, it can be stated first that the findings of the original survey were reproduced and thus reinforced in the follow-up study, using a control group which differed by 50% from the original control group. It was again found with statistical means that in all aspects of oral health and dental status (i.e., the state of remaining teeth and

periodontium, extent of restorative and prosthetic treatment), patients with epilepsy show a significantly worse condition compared with an age-matched group of general (none-epilepsy) population. Upon follow-up, significant deterioration was observed in the dental indices describing the number of missing teeth, state of remaining teeth and the periodontium in both the epilepsy and the control group. This comes as no surprise, as with time the dental status tends to deteriorate in most individuals. However, even the rate of worsening was a significantly higher in patients with epilepsy as compared to the original control group. Furthermore, there was a significant difference in oral hygiene as well, epilepsy patients showing deterioration, control subjects showing improvement. In our first study, we have named a number of possible causes for the observed unfavourable results with respect to epilepsy patients. Some are directly connected with their seizure condition, such as oral cavity injuries and increased exertion on the teeth (Jacobsen and Eden 2008, Buck et al. 1997) or the nowadays rare phenytoin related gingival side effect (Dahllöf et al. 1993, Angelopoulos et al. 1975a, Angelopoulos et al. 1975b), whereas others are only indirectly the consequence of the disease, e.g. socioeconomic-educational background of patients, high rate of unemployment, reimbursement policy and attitude of dentists (Károlyházy et al. 2003). If the present results are contrasted to the improved seizure condition of patients, with an even higher proportion of patients becoming seizure-free, it follows that the disease-specific factors probably play a lesser role in the poor oral health of these patients. The socioeconomic condition of patients and educational factors appear to be more important in explaining these unfavourable results. In support of this statement, our survey also showed that the proportion of employed patients decreased significantly in spite of improvement in their condition.

It is seen in *Table 2* that the difference between the epilepsy and the control group is most pronounced in indices describing oral hygiene and the state of the periodontium, with significant difference even in the rate of worsening (*Fig. 2*). The state of periodontium seems to be the main factor responsible for the unfavourable dental status. A poor periodontal condition

is a risk factor of tooth loss, thus it predicts the deterioration of the DMF-T index as well. Consequently, every effort should be made to improve – among others - the periodontal condition of patients. This involves patient education with the cooperation of the caring neurologist and the dentist, and also education of the dentist himself/herself about the nature of epilepsy and the special needs of these patients. The use of local anti-inflammatory and antiseptic preparations is encouraged. On the other hand, it must be stressed that the majority of patients with epilepsy (about 65-70%) are seizure-free, thus their oral status is unaffected by seizures and possible injuries. Furthermore, AED related side effects are also no longer an issue in this respect, with the possible exception of AED related decrease of bone mass of the mandible (Verroti et al. 2002, Sato et al. 2001). It follows that the majority of patients may and should receive dental treatment that is both aesthetically and functionally identical with the treatment of non-epileptic patients, without specific restrictions. This attitude will also contribute to the improvement of oral health of patients with epilepsy.

References

Angelopoulos AP (1975) Diphenylhydantoin gingival hyperplasia: a clinicopathological review: 1, Incidence, clinical features and histopathology. *J Can Dent Assoc*; 41:103–6.

Angelopoulos AP (1975) Diphenylhydantoin gingival hyperplasia: a clinicopathological review: 2, Aetiology, pathogenesis, differential diagnosis and treatment. *J Can Dent Assoc*; 41:275–7, 283.

Buck D, Baker GA, Jacoby A, Smith DF, Chadwick DW (1997) Patients' experiences of injury as a result of epilepsy. *Epilepsia*; 38:439–44.

Dahllöf G, Preber H, Eliasson S, Rydén H, Karsten J, Modéer T (1993) Periodontal condition of epileptic adults treated long-term with phenytoin or carbamazepine. *Epilepsia*; 34:960–4.

Friedlander AH, Cummings JL (1989) Temporal lobe epilepsy: its association with psychiatric impairment and appropriate dental management. *Oral Surg Oral Med Oral Pathol*; 68:288–92.

Jacobsen PL, Eden O (2008) Epilepsy and dental management of the epileptic patient. *J Contemp Dent Pract;* 9:54-62.

Károlyházy K, Kivovics P, Fejérdy P, Arányi Z (2005) Prosthodontic status and recommended care of patients with epilepsy. *J Prosthet Dent*; 93:177-82.

Károlyházy K, Kovács E, Kivovics P, Fejérdy P, Arányi Z (2003) Dental status and oral health of patients with epilepsy: an epidemiologic study. *Epilepsia;* 44:1102-1107.

Ogunbodede EO, Adamolekun B, Akintomide AO (1998) Oral health and dental treatment needs in Nigerian patients with epilepsy. *Epilepsia*; 39:590–4.

Sato Y, Kondo I, Ishida S, Motooka H, Takayama K, Tomita Y (2001) Decreased bone mass and increased bone turn over with valproate therapy in adults with epilepsy. *Neurology*; 57:445-449.

Shaw MJ, Shaw L, Foster TD (1990) The oral health in different groups of adults with mental handicaps attending Birmingham (UK) adult training centres. *Community Dent Health*; 7:135–41.

Verroti A, Greco R, Latini G, Morgese G, Chiarelli F (2002) Increased bone turn over in prepubertal, pubertal, postpubertal patients receiving carbamazepine. *Epilepsia*; 43:1488-1492.

Westphal P (1972) Dental care of epileptics. *Epilepsia;* 13:233–7.

World Health Organization (1997) *Oral health surveys: basic methods*. 4th ed. Geneva: World Health Organization.

Table 1. Dental classification of epilepsy patients and recommended care

Dental group	Criteria for entrance	Recommended dental care
Group I	• Patients who have been seizure free for years, either with or without medication • Patients with rare seizures (less often than once a year) • Patients exclusively with seizures that do not involve the masticatory apparatus (absence, myoclonus, and certain partial seizures)	No special needs
Group II	• Patients with frequent partial seizures involving the masticatory apparatus, accompanied by clonic movements of facial and masticatory muscles or oral automatisms (e.g., grinding of teeth). • Generalised tonic–clonic seizures, if present, appear less often than once a year	• More resistant restorative materials • Avoid replacement of edges and ceramic inlays
Group III	• Patients with frequent generalized tonic–clonic seizures (more often than once a year)	• Fixed prosthetics • Precision attachments of partial removable dentures • Metal plates for complete dentures
Group IV	• Patients with mental disability, precluding compliance • during dental treatment	Minimum interventions

Table 2. Summary of results of the dental indices

Dental index	Epilepsy group	Control group	Comparison of epilepsy and control group	Epilepsy group Comparison to previous study	Control group Comparison to previous study	Comparison of change between epilepsy and control group
OHI-S	3.89±1.4	1.96±1.1	p<0.0001*	Worsened p<0.001*	Improved p<0.003*	p<0.0001*
DMF-T	20.8±7.7	15.9±7.1	p=0.0002*	Worsened p<0.0001*	Worsened p<0.0001*	non-significant
Abrasion (deep) (%)				Worsened	Worsened	non-significant
Upper teeth	15.8	3.3	p<0.0001*	#	p=0.003*	
Lower teeth	23	7.5	p<0.0001*	p=0.0016*	p=0.003*	
CPITN	3.46±1.19	2.15±0.88	p<0.0001*	Worsened p<0.0001*	Worsened p=0.0111*	p=0.0004*
Periodontal attachment loss (PAL)	3.32±2.3	1.62±1.2	p<0.004*	Worsened p<0.0001*	Worsened p<0.004*	p=0.0058*
Mühlemann index	2.46±3.52	1.01±0.77	p=0.0016*	Worsened p=0.01*	Worsened p=0.009*	non-significant
Prosthetic Index	0.39±0.43	0.55±0.47	p=0.037*	non-significant	non-significant	non-significant

Given values are group means±standard deviations (with the exception of abrasion)

*significant difference

#sample number too low for statistics

OHI-S: Greene-Vermillon Oral Hygiene Index

DMF-T: Index of Decayed, Missing and Filled Teeth

CPITN: Community Periodontal Index of Treatment Needs

Figure 1. Distribution of patients with epilepsy in the different 'dental' subgroups

Note the favourable change upon follow-up: more patients are classified in Group I as a result of reduction of seizure frequency.

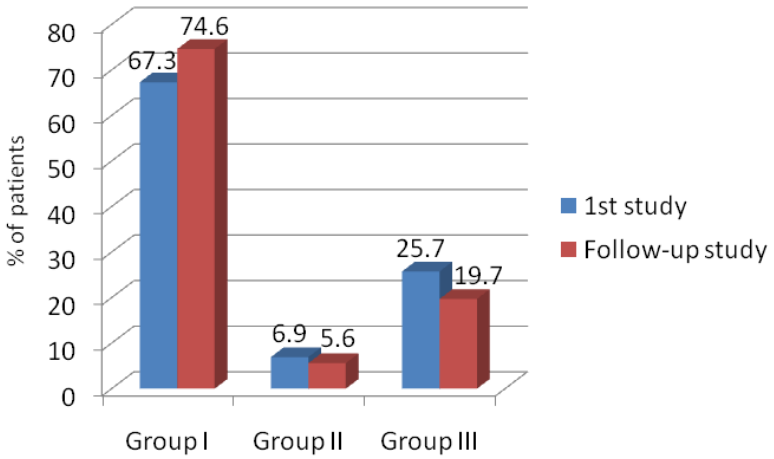

Figure 2. Increase of periodontal attachment loss (PAL) between the first and second surveys in followed-up epilepsy and followed-up control subjects