Original Article

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Gingival Enlargement and Seizure-related Oro-dental Injuries in Patients with Epilepsy

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Abstract

Background: Patients living with epilepsy suffer from the adverse effects of antiepileptic medication such as gingival enlargement and traumatic injuries of the oral cavity related to the epileptic seizures. This study aimed to assess the prevalence of gingival enlargement and seizure-related oro-dental injuries among patients with epilepsy.

Materials and Methods: This descriptive cross-sectional study included 500 consecutive patients with epilepsy attending the Outpatient Department of Neurology at a tertiary care hospital in Bengaluru, India. Patients were categorized into four groups according to the dental risk factors and manageability.

Results: Gingival enlargement was observed in 59% of patients on phenytoin (PHT) therapy. Among them, 33% of patients were on PHT monotherapy and 67% were on PHT polytherapy. Of the 120 subjects with gingival enlargement, 49% had moderate enlargement while 10% had a severe enlargement. Oro-mucosal injuries were significantly more in the study population as compared to injuries of the teeth and jaws. This comparison across the groups was statistically significant ($P < 0.03$). Trauma to the tongue, cheek biting, lip injury, fracture and loss of teeth, and jaw fractures were seen only in patients with generalized tonic-clonic seizures (Groups II, III, and IV). Lip injury, cheek biting, trauma to tongue, loss of teeth, and jaw fracture were all significantly associated ($P < 0.05$) with seizures occurring more than once a year.

Conclusions: The prevalence of gingival enlargement and seizure-related hard and soft tissue injuries of the oral cavity in patients with epilepsy supported the need for an interdisciplinary approach and targeted oral health promotion to ameliorate the oral health of these patients with epilepsy.

Key words: Antiepileptic drugs, Dental injury, Epilepsy, Fracture, Gingival enlargement, Seizure

INTRODUCTION

Gingival overgrowth (GO) or gingival enlargement is one of the most frequent and troublesome adverse effects associated with the administration of the anticonvulsant drug phenytoin (PHT), calcium channel blockers such as nifedipine, and the immunosuppressant cyclosporine.[1] It has been reported to occur in 16-94% of patients treated with PHT.[2] Gingival enlargement is also a side effect of other antiepileptic drugs (AEDs) such as barbiturate, sodium valproate, carbamazepine, and vigabatrin therapy. Clinical manifestation of gingival enlargement frequently appears within 1-3 months after initiation of treatment with the associated medications. GO normally begins at the interdental papillae and is more frequently found in the anterior segment of the labial surfaces. Gradually, gingival lobulations are formed that may appear inflamed or more fibrotic in nature, depending on the degree of local factor-induced inflammation.[3] The fibrotic enlargement normally is confined to the attached gingiva but may extend coronally and interfere with esthetics, mastication, or speech. Disfiguring GO triggered by these medications is not only displeasing but often impairs nutrition and access for oral hygiene, resulting in retention of food

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and debris, halitosis, an increased susceptibility to oral infections, caries, and periodontal diseases.[3] The gingival tissue overgrowth may also lead to delayed eruption of the teeth and sometimes malalignment of teeth.[4]

Patients with epilepsy have increased the risk of dental and maxillofacial trauma. Falls during seizures can cause soft tissue lacerations, facial fractures, temporomandibular joint subluxation, and devitalization, fractures, and subluxation or avulsion of teeth.[5] In a report, the proportion of people who sustained various injuries during a seizure and had at least one seizure during the previous year was: 24% sustained at least one head injury, 16% sustained a burn or scald, 10% a dental injury, and 6% some other fracture.[6] Studies have shown an increased prevalence of traumatic anterior dental injuries in patients with epilepsy as compared with the prevalence reported for those without epilepsy.[7] In patients with epilepsy and AEDs, the incidence of fractures is 2-6 times higher compared to the general population.[8] Relatively, little has been reported in the literature about the incidence and nature of non-fatal seizure-related injuries of the craniofacial complex, especially the oro-dental injuries among the patients living with epilepsy in India.

This study was carried out to assess the oral health status and dental treatment needs and also the seizure-related injuries of the oral cavity, among patients living with epilepsy, who attended the Outpatient Department of Neurology at a tertiary care government teaching hospital in Bengaluru, Karnataka, India. The prevalence of gingival enlargement and seizure-related oro-dental injuries is reported in this paper; the oral health status and dental treatment needs will be described in a subsequent publication.

MATERIALS AND METHODS

This descriptive cross-sectional study was carried out on 500 consecutive epileptic patients visiting the Outpatient Department (OPD) of the Department of Neurology of a tertiary care Government teaching hospital in Bengaluru city, during 2008-2009. Patients fulfilling the following eligibility criteria were included in the study: Persons aged above 5 years, diagnosed with epilepsy as per the case definition of epilepsy given by the Commission on Epidemiology and Prognosis, International League Against Epilepsy,[9] who had been under treatment for at least six months duration (as per the patients' case records) before the day of dental examination. Individuals who had only febrile seizures or only neonatal seizures, and those who were concurrently on other medications known to cause gingival enlargement and were not included in the study. Informed consent and ethical clearance were obtained.

The clinical and diagnostic features of the patient's epilepsy were sought from the case records and from interviewing the patients if required. A specially designed proforma in a structured questionnaire format was used to collect information on patients' demographic details, oral hygiene practices, epileptic history (age of onset, most recent occurrence of seizure, type and frequency of seizure, time of attacks, aura, involvement of masticatory system, AED therapy), including details of seizure-related injuries to the oral cavity, visits to dentist, and categorize patients into 4 groups according to the dental risk factors and manageability. Epileptic patients were categorized, with the help of the neurologist, into dental subgroups, as given in the classification by Károlyházy *et al.*[10]

The oral examination of all patients was carried out in the Outpatient Department of the Department of Neurology, Victoria hospital, by a single investigator (S.S.Y) after calibration to limit intra-examiner variability. Information on gingival enlargement was recorded on the WHO oral health assessment form (1997),[11] and the grading for gingival enlargement was done as follows: The dentition was divided into six sextants as used for the Community Periodontal index (CPI index).[11] Probing depth (PD) measured by a CPI probe (Hu-Friedy) was used as a marker of the development and progression of gingival enlargement (none: PD $\leq$ 3 mm, moderate: PD 3-5 mm, and severe: >5 mm). The tooth with the most serious gingival condition in each sextant was selected as representative.[1]

The data were analyzed using SPSS 15.0 software package. Univariate and Bivariate frequency tables were generated with percentages for comparison of various categories between groups. Descriptive statistics were computed for continuous variables studied. Association for some key variables and groups were studied using Chi-square test statistic with appropriate degrees of freedom. Z-test for proportion based on binomial distribution has been used to find the significance of association of seizure-related injuries with the study characteristics. Any $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 500 patients with epilepsy, in the age range of 5-85 years, were examined, out of which 302 (60.4%) were males (mean age 30.80 $\pm$ 14.18 years) and 198 (39.6%) were females (mean age 28.48 $\pm$ 11.57 years). As per the classification of patients based on dental risk factors and manageability, the study subjects belonged to one of the 4 groups as follows: 8% (n = 40) were in Group I, 68.2% (n = 341) in Group II, 20.4% (n = 102) in Group III, and 3.4% (n = 17) in Group IV.

Gingival Enlargement

Gingival enlargement was observed in 120 (59%) of the 203 patients on PHT therapy. Based on the severity of gingival enlargement, none or no enlargement was present in 83 patients (41%); moderate gingival enlargement was seen in 99 subjects (49%), and severe enlargement of the gingiva was noted in 21 (10%) of the 203 study subjects all of whom were on treatment with PHT therapy. Of the 120 patients who presented with gingival enlargement, 33% were on PHT monotherapy, and the rest (67%) were on PHT polytherapy/multi-drug therapy, i.e., in combination with phenobarbitone (PB) in most cases, or a combination of PHT, PB, and carbamazepine in a few cases.

Seizure-related Injuries of the Oral Cavity

The prevalence of seizure-related injuries of oral cavity and jaw bones showed that 46.8% had no injury, 14% had cheek biting, 46% had tongue bite, 5.2% had lip injury, 7.2% had fractured teeth, 6.8% had loss of teeth, and 1% had jaw fracture. The percentages do not add up to 100 as some subjects had more than one type of injury. Group I patients did not experience any injuries. The distribution of the number of subjects by seizure-related injuries of the oral cavity, across the four subgroups, is shown in Table 1.

Cheek biting had been experienced by more number of subjects from Group II. Trauma to tongue during seizures was the most common injury among the study population and had occurred in 230 (46%) subjects. Lip injury had occurred in more number of subjects in Group III and Group II (Table 1).

Fracture of teeth due to seizure-related injury had occurred in a greater number of patients from Group II, whereas loss of teeth as a consequence of seizures had occurred in an equal number of subjects in Groups II and III. Fracture of teeth involved the anterior teeth in all cases except three subjects: Two subjects with molar fractures and one with premolar fracture; loss of teeth also involved the anterior teeth in all cases, except four cases which also involved loss of posterior teeth (loss of premolars in two subjects and loss of first molar teeth in two subjects).

Fracture of the jaws due to seizure-related injury had been recorded in five patients, out of whom one belonged to Group II and four belonged to Group III (Table 1).

The association, if any, between age, gender, duration of seizure, frequency of seizures, and time of attacks with the various seizure-related injuries was explored. A significant association was seen between the age groups of 31-40 years and seizure-related injury ($P < 0.05$), particularly, cheek biting ($P < 0.05$) and trauma to tongue ($P \leq 0.01$). The association between fracture of teeth and ages 51-60 years was significant ($P < 0.05$) while that between gender and the seizure-related injury was not significant. The associations between fractures of the jaw and ages 51-60 years and duration of seizure and trauma to tongue and fracture of teeth were suggestive of statistical significance. The frequency of seizures of more than once a year ($P \leq 0.01$) and one or more seizures a month ($P < 0.05$) was related to seizure-related injuries (Table 2). The association of lip injury to a seizure frequency of more than once a year was highly significantly ($P \leq 0.01$). Cheek biting, trauma to tongue, loss of teeth, and jaw fracture were all significantly related ($P < 0.05$) to seizures occurring more than once a year. Frequent seizures of one or more a month were significantly associated ($P < 0.05$), with seizure-related injury and loss of teeth in particular.

The association between time of attack and seizure-related injury is shown in Table 3. Statistical significance ($P < 0.05$) was noted only in case of seizure-related injury, especially trauma to the tongue and nocturnal attacks. Both diurnal and nocturnal attacks were significantly related to cheek biting and statistical significance was suggested in case of the association between fracture of teeth and such unpredictability of time of attack.

DISCUSSION

The severity of gingival enlargement noted in the present study is comparable to that described by Akiyama *et al.*[1] However, of the 120 patients who presented with gingival enlargement, 33% were on PHT monotherapy, akin to the results of a Nigerian study;[7] and the rest (67%) were on PHT multi-drug therapy, i.e., in combination with PB in most cases, or a combination of PHT, PB, and carbamazepine in a few cases.

Numerous reports suggest that young age is an important risk factor in PHT-induced gingival enlargement.[12] Since

Table 1: Distribution of subjects by seizure-related injuries of the oral cavity

Injuries		None	Cheek biting	Trauma to tongue	Lip injury	Teeth fracture	Loss of teeth	Jaw fracture
Group I (*n*=40)	No.	40	0	0	0	0	0	0
Group II (*n*=341)	No.	162	42	152	10	25	14	1
Group III (*n*=102)	No.	25	24	68	12	10	14	4
Group IV (*n*=17)	No.	7	4	10	4	1	1	0
Total	No.	234	70	230	26	36	29	5

Numbers do not add up to 500 as some subjects had more than one condition

Table 2: Association of frequency of seizure and related injury

Frequency of seizure	Total number of patients	No injury	Injury	Cheek biting	Trauma to tongue	Lip injury	Fracture of teeth	Loss of teeth	Jaw fracture
None in past year	3	2 (66.7)	1 (33.3)	0	1 (33.3)	0	0	0	0
Less than once a year	362	189 (52.2)	173 (47.8)	43 (11.8)	147 (40.6)	11 (3.1)	25 (6.9)	15 (4.1)	1 (0.3)
More than once a year	98	33 (33.7)	65** (66.3)	21* (21.4)	57* (58.2)	11** (11.2)	8 (8.2)	13* (13.3)	3* (3.1)
One or more a month	37	10 (27.1)	27* (72.9)	6 (16.2)	25 (67.6)	4 (10.8)	3 (8.1)	6* (16.2)	1 (2.7)
Total	500	234 (46.8)	266 (53.2)	70 (14.0)	230 (46.0)	26 (5.2)	36 (7.2)	34 (6.8)	5 (1.0)

*P<0.05, **P<0.01; Figures in parenthesis indicate percentages

Table 3: Association of time of epileptic attack and related injury

Time of attack	Total number of patients	No injury	Injury	Cheek biting	Trauma to tongue	Lip injury	Fracture of teeth	Loss of teeth	Jaw fracture
Diurnal	230	130 (56.5)	100 (43.5)	19 (8.3)	85 (36.9)	10 (4.3)	17 (7.4)	17 (7.4)	2 (0.9)
Nocturnal	149	57 (38.3)	92* (61.7)	26 (17.4)	83* (55.7)	7 (4.7)	5 (3.4)	8 (5.4)	1 (0.7)
Both diurnal and nocturnal	121	47 (38.8)	74 (61.2)	25* (20.7)	62 (51.2)	9 (7.4)	14 (11.6)	9 (7.4)	2 (1.7)
Total	500	234 (46.8)	266 (53.2)	70 (14.0)	230 (46.0)	26 (5.2)	36 (7.2)	34 (6.8)	5 (1.0)

*P<0.05, Figures in parenthesis indicate percentages

58% of the study population was below the age of 30 years (the mean age of the total population was 29.49 [±13.25] years), it is a likely explanation for the prevalence of gingival enlargement seen in patients on PHT therapy in the present study. However, this relation between age and gingival enlargement was not statistically analyzed as it was not one of the objectives of the study. Similar findings as in the present study were observed by Majola *et al.*[12] in the South African outpatient population (62% prevalence, mean age of population was 33.6 years and statistically significant relation to age was seen) and also among Indian children (57% prevalence, age range 8-13 years) with epileptic disorders and receiving monodrug therapy with PHT, at Post Graduate Institute of Medical Education and Research, Chandigarh (PGIMER).[13]

Firm evidence of the involvement of PHT as the principal iatrogenic factor in the development of gingival enlargement has been presented in the literature. Similar to the Nigerian study,[7] none of the patients receiving PB as monotherapy manifested the disorder. Therefore, PB appears to potentiate the effect of PHT in causing gingival enlargement. Contrastingly, in the Yelandur study gingival enlargement was noted in 4% of patients on phenobarbital and 43% of those on PHT.[14] These differences may be due, at least in part, to the assessment of enlargement by medical (i.e., non-dental) personnel, differing indices of overgrowth and a community-based study population. The exact role of PB alone and in combination with other anticonvulsants in causing enlargement of gingival tissues needs to be elucidated, especially in the local epileptic population, since the drug is widely used here. PB was observed to be the most commonly used the antiepileptic drug in the present study. Good plaque control, removal of plaque retentive factors and treatment of any underlying periodontal condition will reduce gingival inflammation and hence the severity of any drug-induced GO.[15] A 3-month interval for periodontal maintenance therapy has been recommended for patients taking drugs associated with gingival enlargement.[16]

The assessment of seizure-related injuries ever experienced by the study population showed that many (n = 234) of the subjects had not experienced any seizure-related injuries of the oral cavity and especially those from Group I were free of such injuries. This could be because subjects from Group I had seizures without falls and effect on the teeth (masticatory system). Oro-mucosal injuries were significantly more in the study population as compared to injuries of the teeth and jaws, and this comparison across the groups was also statistically significant (P < 0.03). Trauma to tongue during seizures was the most common injury among the study population and had occurred in 230 subjects. This is similar to the study of Roberge and Maceira-Rodriguez where the tongue was the most common site of injury among those with generalized seizures and 48 of 52 seizure-related oral lacerations involved the tongue.[17] In the present study, trauma to tongue, cheek biting, and lip injury was reported by patients with grand mal convulsions and hence seen only among subjects from Groups II, III, and IV. Fracture and loss of teeth and jaw fractures were also seen only in patients with generalized tonic-clonic seizures (Groups II, III, and IV). This is in accordance with previous observations that generalized tonic-clonic seizures very often cause minor oral cavity injuries, such as biting of the tongue or other areas of the oral mucosa, but frequently lead to injuries of the teeth and sometimes also cause fractures of jaws and other extremities.[17] The finding that fracture and loss of teeth predominantly

affected the anterior teeth in the present study is similar to that reported in the Nigerian study.[7] In the study by Buck *et al.,* 28 of 344 epilepsy patients had seizure-related tooth injuries within 1 year.[6] These might occur as a result of the fall or of the forceful contraction of the masticatory muscles during both the tonic and clonic phases. Thus, the exertion and risk of injury of the teeth of patients with frequent generalized tonic-clonic seizures (Group III) are very much increased, contributing to the compromised dental health status.[10]

The association, if any, between age, gender, duration of seizure, frequency of seizures, and time of attacks with the various seizure-related injuries was explored. The association between fracture of teeth and ages 51-60 years was significant ($P < 0.05$), whereas that between gender and the seizure-related injury was not significant, which is in accordance with the study of Tiamkao and Shorvon.[18] The frequency of seizures of more than once a year ($P \leq 0.01$) and one or more seizures a month ($P < 0.05$) was definitely related to seizure-related injuries, and this finding is supported by other studies; the study by Buck *et al.* showed that seizure severity, type, and frequency were the best predictors of all types of injury (head injury, burns/scalds, dental injury including loss of teeth, jaw fracture, admission to hospital and major dental surgery, other fractures, and seizures while bathing/swimming) and having tonic-clonic seizures or the combination of tonic-clonic and other seizures and at least three drug-related adverse effects significantly increased the chances of sustaining dental trauma.[6] Lip injury, cheek biting, trauma to tongue, loss of teeth, and jaw fracture were all significantly associated ($P < 0.05$) with seizures occurring more than once a year. Frequent seizures of one or more a month were significantly associated ($P < 0.05$) with seizure-related injury and loss of teeth in particular. The study by Tiamkao and Shorvon also reported that significant risk factors for injury were generalized tonic-clonic seizures, high frequency of seizures, and seizures with a fall.[18]

Thus, the classification of epileptic patients[10] used in the present study makes it useful for the study of seizure-related injuries of the oral cavity. However, a prospective study, wherein patients or care givers could maintain a dairy recording the occurrence of seizures, and seizure-related injuries would reduce recall error, problems of inadequate medical documentation, especially of minor injuries and be better suited to elicit valid and reliable data on the seizure-related injuries of the oral cavity. The present study, being restricted to the hospital outpatients only, may not be adequately representative of all epileptic patients in the community. This limits the generalizability of the findings.

This study is a foray into an area of oral health research that has barely been investigated in the Indian context. The data on seizure-related injuries of the oral cavity add to the sparse literature[19] available in this regard.

CONCLUSION

Interdisciplinary collaboration, referral by the neurologist for preventive dental care including adequate dental plaque control measures as well as thorough examination of the injuries to the oral cavity to rule out occult maxillofacial trauma can help improve the overall health and quality of life of patients with epilepsy.

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