Original Article

Comparative evaluation of oral hygiene status and gingival enlargement among epileptic and healthy children as related to various antiepileptic drugs

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Abstract:

Background: Epilepsy is a gathering of neurological disorders characterized by epileptic seizures. Epileptic children, who are on active treatment with antiepileptic drugs, have a well-recognized side effect of gingival enlargement. Therefore, all efforts should be made, particularly for the population who are diagnosed or affected by the systemic disease. This study was conducted with an aim to determine oral hygiene status and gingival enlargement among epileptic and healthy children as related to various antiepileptic drugs. **Materials and Methods:** The cross-sectional observational study was conducted in the department of pedodontics and attached general hospital. A sample size of 120 participants with 60 healthy and 60 epileptic children between age 2 and 14 years were included. Oral health status of participants was examined using oral hygiene simplified index and plaque index. Gingival enlargement was assessed using Miranda–Brunet index. For statistical analysis, one-way ANOVA test, independent *t*-test, and Pearson's Chi-square test were used. **Results:** From the total participants included in the study, 49% of participants had good oral hygiene from healthy group, and 28% participants had poor oral hygiene from the epileptic group. Sodium valproate was the most common drug used and was associated with increased gingival enlargement. **Conclusion:** Conclusion can be drawn that epileptic children under medication had poor oral hygiene and an increased risk for gingival enlargement as compared to their healthy counterparts. It must be stressed that the epileptic patients should be given dental care without conditions and provided with best possible care to restore esthetics and functions.

Key words:

Dental caries, drug dispense form, epilepsy, Miranda Brunet index, saliva pH

INTRODUCTION

The overall prevalence of epilepsy in general population is 0.9%.[1] The International Classification categorizes epileptic seizures as focal (partial) seizures and generalized seizures. Focal seizures also termed as partial seizures, appears as electroencephalogram (EEG) changes suggestive of initial activation of neurons which is constrained to a part of one cerebral hemisphere; whereas in generalized seizures, changes suggest synchronous involvement of all areas of both hemispheres. Generalized seizures are of different types such as (i) atonic; (ii) tonic; (iii) clonic; (iv) myoclonic; (v) tonic–clonic; or (vi) absence seizures on the basis of clinical features and EEG findings. Generalized tonic–clonic (GTC) seizures also termed as grand mal seizures are considered as theatrical of all medical situations. The first choice of drug for GTC seizures by physician is valproic acid. Phenytoin and carbamazepine are sensible second alternatives. Phenobarbitol is still utilized by numerous neurologists.

Epileptic children, who are on active treatment with antiepileptic drugs, have a well-recognized side effect of gingival enlargement or overgrowth, often designated as gingival hyperplasia. Although the cause of gingival hyperplasia due to drugs have been correlated with multiple

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factors, the exact cause is not yet clear. There are various aspects such as effect of sex, age, duration, and drug dosages which needs to be explored for better understanding of gingival overgrowth pathogenesis.[2] Commonly associated drugs with gingival enlargement belong to two categories, namely, calcium channel blockers and anticonvulsants. According to the literature, gingival growth due to phenytoin has been associated with (i) multiple antiepileptic drugs; (ii) host response; (iii) reduced serum folate levels, and (iv) plaque accumulation.[3] Gingival enlargement causes pseudopockets forming plaque bearing areas, which ultimately enhances the patient's susceptibility to dental caries, inflammation of gingiva and periodontal problems.[4]

There are very few studies done to assess the oral health status and gingival enlargement in epileptic patients undergoing treatment of epilepsy compared to healthy controls. Hence, this study may bring some new insights pertaining to oral health in medically ill children. The main aim of the present study was to determine oral hygiene status and gingival enlargement among epileptic and healthy children as related to various antiepileptic drugs (AED's).

MATERIALS AND METHODS

The proposed study was conducted as a cross-sectional observational study. The study was conducted in the respective institution. Participant selection and data collection were initiated after approval from Institutional Ethics Committee. Informed and written consent was taken from patients/guardians in English/local language (Gujarati) before the examination. Patients were enrolled from November 2015 to May 2016.

A sample size of 120 participants between chronological age of 2–14 years was included in the study. The sample size was determined by following formula.

Formula: $N = 2 \times (Z \times SD/d)^2$

$= 45.94 = 46$ (minimum study sample size for each group) – power 90%.

According to abovementioned formula, the sample size obtained was 46. For equal distribution of samples in subgroups; sample size selected was 60 for healthy and 60 for epileptic children. Age stratification was done, and age-matched healthy controls were selected for the study [Table 1].

The samples were selected considering inclusion and exclusion criteria as mentioned below:

Inclusion criteria for epileptic group

Epileptic children of age group 2–14 years, children on antiepileptic drug therapy for at least 6 months, children with constant GTC seizures (more than one episode per year) and children who have not undergone oral prophylaxis regime in the past 6 months.

Table 1: Sample size distribution

Age (Years)	Epileptic	Healthy
2-6	20	20
>6-10	20	20
>10-14	20	20

Inclusion criteria for healthy group

Healthy children of age group 2–14 years, children free of any diseases and not taking any medication, and children who have not undergone oral prophylaxis regime in the past 6 months.

Exclusion criteria

Physically disabled children and parents not willing to give informed written consent.

The demographic details were collected and entered into the pro forma. The examination was carried out in natural daylight with children seated upright in chair with backrest. Autoclaved diagnostic instruments were used for recording the indices. Principal investigator did all the oral examination and index recording. An assistant was trained to help the principal investigator for data recording purpose.

The examination incorporated the following:

Oral hygiene status

Status of oral health of participants was examined using oral hygiene simplified index (OHI-S Index-given by Greene and vermillion) and plaque index (PI) (Silness and Loe).[5] It was done by inspecting the amount of dental plaque (using no. 23 Shepherd's hook explorer) and calculus (using no. 5 explorer) present individually on each tooth. The calculus and debris scores were aggregated for each individual and division was done by the total tooth surfaces recorded. Separate calculations were carried out, and later on, they were summed to get the OHI-S score. The obtained score were interpreted using the following criteria: Good score (0.0–1.2); fair score (1.3–3.0), and poor score (3.1–6.0). For recording PI, indices for each of the tooth were totaled, and the score was divided by the number of teeth recorded. The scores ranged from 0 to 3, that is, excellent score (0); good score (0.1–0.9); fair score (1.0–1.9); and poor score (2.0–3.0).

Gingival enlargement

It was assessed using Miranda–Brunet index. To estimate the amount of gingival enlargement a standard periodontal probe (Michigan 8/11, Hu-Friedy)[6] was used. The height of enlarged gingival tissue was deliberated from cementoenamel junction to free gingival margin. The increment in size of papilla was calculated from surface of the enamel, at interdental contact point, to outer surface of the papilla. Scores; one for buccal papilla and another for lingual/palatal papilla were obtained, according to the following criteria: Grade 0 (papillary thickness <1 mm), Grade 1(papillary thickness 1–2 mm), and Grade 2 (papillary thickness >2 mm).

Statistical analysis

Data collected were entered in the Master chart prepared using Microsoft Excel 2007, and the data were analyzed using SPSS-21 software (SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Independent *t*-test was used for intergroup comparison of the mean score of various Indices. One-way ANOVA test was used for inter- and intra-group comparison and Pearson's Chi-square test was employed to check the association in between the groups.

RESULTS

Our study group comprised of 120 children; 60 epileptic and 60 healthy participants. From the total participants selected, 66 were male and 54 were female and male to female ratio was 1:1.2 age 2–14 years.

The statistical analysis of data [Graph 1] on oral hygiene status showed that epileptic children had poor oral hygiene as compared to healthy controls. *P* value, as determined by Pearson's Chi-square test was found to be highly significant (<0.001).

The statistical analysis of data [Graph 2] on PI score showed that 53.3% (32) participants had good oral hygiene status from healthy group, whereas only 3% (5) participants from epileptic group had good oral hygiene status. The *P* value, as determined by Pearson's Chi-square test was found to be highly significant (<0.001).

The epileptic children had high Miranda–brunet Index score than healthy children. The mean score for epileptic children was 1.75, whereas for healthy children it was 0.33. Furthermore, the *P* value was found to be highly significant (<0.001) calculated according to Pearson's Chi-square Test [Graph 3].

Positive correlation was found between drug dispense form and intensity of gingival enlargement [Table 2].

The results show that sodium valproate is the most commonly used drug and is responsible for gingival enlargement.

Table 2: Correlation of drug dispense form and gingival enlargement

Drug Dispense	Miranda Brunet Index				
	Grade 0	Grade 1	Grade 2	Grade 3	Total
Capsule	1	0	1	0	2
Syrup	0	2	3	1	6
Tablet	2	9	18	7	36
Tablet + syrup	2	5	6	3	16

Pearson's Chi-square shows p-value to be highly significant (<0.001)

Table 3: Drug combination and gingival enlargement

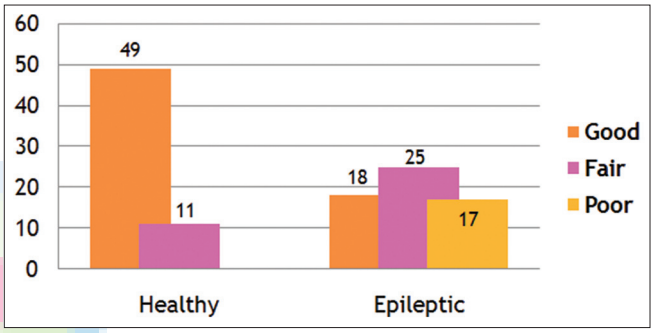
Medication	Miranda Brunet Index				
	Grade 0	Grade 1	Grade 2	Grade 3	Total
Clobazam	0	1	1	1	3
Clobazam + Topiramate	0	0	0	1	1
Clobazam + Sodium Valproate	1	2	10	3	16
Clobazam + Valproate	0	1	0	0	1
Clonazepam + Phenobarbitol	0	0	1	0	1
Lamotrigine + Sodium Valproate	0	1	0	0	1
Phenobarbitol	0	1	1	1	3
Sodium Valproate	3	5	11	4	23
Sodium Valproate + Carbamazepine	1	1	0	0	2
Sodium Valproate + Clobazam	0	0	0	1	2
Sodium Valproate + Clonazepam	0	2	1	0	3
Sodium Valproate + Topiramate	0	1	1	0	2
Topiramate	0	0	2	0	2

Following this, combination of clobazam and sodium valproate is also prescribed often and it also has side effects like gingival enlargement [Table 3].

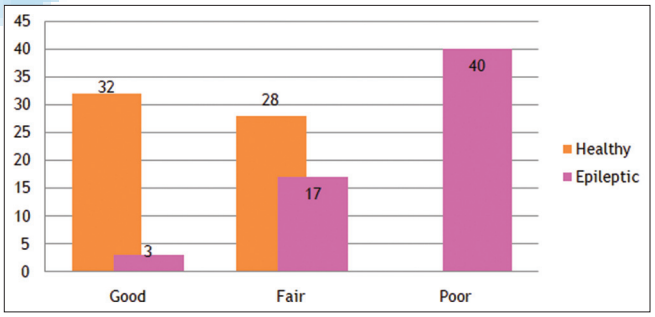
DISCUSSION

Epilepsy is relatively a prevalent disease in children. Dentists' frequently come across with epileptic patients in their practice and is considered as the second most common medical condition reported in the dental office.[1] Dentists' should be aware of various presentations of the disease, anticonvulsant drugs taken by the patient, complications and adverse effects of these medications.

The results of the current study demonstrate that, oral hygiene and dental status, in epileptic children showed a significant difference compared with an age-matched healthy (nonepileptic) population. Majority of children in the present study never consulted a dentist in the past. This may be explanation of inadequate oral hygiene in epileptic



Graph 1: Comparison of oral hygiene status between healthy and epileptic group



Graph 2: Comparison of the plaque index score between healthy and epileptic group

Graph 3: Comparison of Miranda–Brunet index score between healthy and epileptic group

population. Ignored oral hygiene, injuries to oral cavity, and increased strain on teeth if presented together can result in poor oral health. Regular long-term consumption of drugs which usually contains sugar increases the risk of impaired oral health in epileptic children. Hence, it is challenging to maintain proper oral hygiene in these patients. Hence, it is of utmost importance to plan dental treatment carefully and emphasize on preventive treatment protocol for children diagnosed with epilepsy.

The pessimistic demeanor of dentists can also be a restricting reason in providing optimal dental therapy. Many times dentists pick therapy options that are fast and uncomplicated, such as extraction. The various reasons associated with such attitude are lack of proper knowledge about the disease and seizure phobia which may occur during procedure and underequipped set up for dealing such emergency situations.[7]

Most of the epileptic patients can be treated successfully with AEDs. Rarely, neurosurgery or vagus nerve stimulation is needed. The later therapy options depend on the severity and type of epilepsy. In Europe and North America, more than 15 AEDs have been given approval for the management of epilepsy.[8] To control their seizures polydrug therapy is often indicated: Less than or equal to 50%, attain control with 1 drug therapy; 2 drugs are required only in 10% cases, whereas 5% epileptic patients respond to 3 or 4 combinations of drug.[9] The quality of life of epileptic children gets affected due to deterioration in their oral health along with systemic and social problems.

Gingival hyperplasia is the most explored periodontal condition, widely associated with epilepsy. Phenytoin (Eptoin) is an antiepileptic drug frequently needed to treat epileptic children. The effect of drug dosage on the development of gingival hyperplasia is partially understood, and inferences made in reports are not in absolute consensus to, if the gingival adversities in phenytoin-treated epileptics are due to its saliva or plasma levels or not.[10-12] Reported incidences by Angelopoulos and Hassell *et al*. gave a range between 0% and 84.5%, but the majority of researchers believe that 50% of patients taking phenytoin develop hyperplasia.[13,14] Other commonly prescribed AEDs, such as barbiturates (phenobarbitone [Gardenal]), primidone (Mysoline), and valproic acid (Valparin), rarely cause mild gingival hyperplasia.[15-18]

The study done by Lundström *et al*. demonstrated that children and adolescents who took phenytoin develop larger number of gingival units with increase in depth of probing than individuals given carbamazepine during comparable period.[19] Findings in our study support previous reports that gingival enlargement seen in children on phenytoin medication is linked with the deposition of plaque in dentogingival areas with simultaneous inflammation of gingiva.[20,21] Nonmodifiable factors such as genetic factor, age, and sex can predict individual's inherent risks for gingival hyperplasia.[12,20]

Valproate is a broad-spectrum antiepileptic drug used as a drug of choice for almost three decades as mentioned by Brodie and Dichter.[22] Irrespective of type of epilepsy including absence, GTC seizure, and myoclonic seizures, it is considered best treatment options by the clinicians. Eeg-Olofsson *et al*. studied the outcome of valproic acid salts on ten children between 8 and 14 years old having epilepsy; and found no periodontal adverse effects on teeth in good health.[23] In addition, Seymour *et al*. revealed that valproic acid had no ill effects on the periodontal health of the 15 adult epileptic patients between 17 and 68 years old.[24] The results of the study may differ due to the difference in the age group selected. It has been found that gingiva is more susceptible to valproic acid in younger patients. Using antiepileptic drugs in solo therapy or polytherapy might be a reason in the development of gingival enlargement. Ogunbodede *et al*. mentioned that 33.3% of epileptics with phenytoin alone developed gingival hyperplasia and that the fraction goes up to 83.3% when patients received phenytoin with phenobarbitone.[7] Monotherapy with phenobarbitone did not cause gingival hyperplasia; they came to a conclusion that phenobarbitone potentiated the side effect of phenytoin. According to the study done by Gurbuz and Tan, gingival hyperplasia was found in 42% of epileptics on valproic acid, 16% in patients using phenobarbitone, and nil on carbamazepine.[25]

Elimination of local irritants can prevent gingival enlargement. Measures such as regular dental care and a well-established follow-up protocol for oral hygiene reinforcement during foremost 12 months of treatment with phenytoin should be carried out.[26] For first 6 months monthly and in every 3 months, one-time recall can effectively prevent inflammation and hyperplasia. Care at home should have an intrasulcular method of brushing the teeth and thorough cleansing interdentally for getting best outcomes.[27]

This study has shown the necessity for good interaction between dentists and physicians in treatment planning of epileptics. Physicians and pediatricians must be vigilant regarding the oral health and should consult periodontist and pedodontist when needed. Based on the present findings, it can be stated that epileptic children having oral diseases have increased the risk of getting dental conditions as compare to healthy controls. Hence, we need to improve hygiene of oral cavity in epileptic children to prevent periodontal diseases and dental caries.

Limitation

The age group selected (2–14 years) could have variability in oral hygiene method, duration, interval, and parental assistance which might influence the observation in the study.

CONCLUSION

Specific guidelines in oral health are necessary to counterbalance with the raised number of cases of gingival enlargement in epileptic children. To avoid dental disease in the future and progression of disease; a well-structured follow-up protocol should be formulated in the management of oral conditions in epilepsy. Pediatric dentist and dental practitioners should accentuate to enlighten such group regarding oral health and hygiene. There is a need for training programs to be held for maintaining the oral health by school teachers as well as for parents of these patients. Early prevention and intervention shall be the hallmark of good oral health status for these children growing in adults.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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