Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Role of Cumulative Anti-epileptic Drug Load on the Periodontal Health Tissues and Seizure Related Traumatic Oro-dental Injuries – A Comparative Cross-sectional Study in a Tertiary Health Institution in Jammu City

Nanika Mahajan[1], Palak Mahajan[2], Abhishek Khajuria[3], Bhanu Kotwal[4], Bhavana Kaul[5], Rakesh Gupta[6]

[1]Lecturer, Department of Pedodontics and Preventive Dentistry, Indira Gandhi Government Dental College, Jammu, Jammu and Kashmir, India, [2]Research Sc holar, Department of Computer Science and IT, University of Jammu, Jammu, Jammu and Kashmir, India, [3]Resident, Department of Dentistry, Government Medical College, Kathua, Jammu and Kashmir, India, [4]Lecturer, Department of Periodontics, Indira Gandhi Government Dental College, Jammu, Jammu and Kashmir, India, [5]Associate Professor, Pedodontics and Preventive Dentistry, Indira Gandhi Government Dental College, Jammu, Jammu and Kashmir, India, [6]Professor, Pedodontics and Preventive Dentistry, Indira Gandhi Government Dental College, Jammu, Jammu and Kashmir, India

Abstract

Introduction: Epilepsy is one of the most common neurological disorders. Recurrent episodes of seizures put patients at a higher risk of suffering orofacial injuries. The anti-epileptic drugs (AEDs) used to control seizures have been found to cause many adverse effects in the oral cavity.

Objective: The objective of the study was to assess the role of AEDs on dental health and frequency of seizure related head and intra-oral traumatic injuries.

Study Design/Materials and Methods: A comparative study was conducted between epileptic children and a control group which was formed from non-epileptic patients. The two groups were compared with regard to side effects of AEDs and orodental injuries. For statistical analysis, Pearson's Chi-square test was used to evaluate the correlation between the two groups.

Results: The common oral side effects of AED drugs seen were xerostomia, gingivitis, gingival hyperplasia, and glossitis. The epilepsy patients significantly showed more AED side effects as well as more trauma. The most common intra-oral injuries seen in epilepsy group were lips/cheek bite 28.7%, tongue injuries 33%, tooth cracked 37%, and tooth fracture 25.3%. Some children witnessed temporomandibular joint injuries, nose fractures, eye socket trauma, and even skull crack.

Conclusion: Epileptic children under medication had poor oral hygiene and an increased risk of gingival enlargement. Traumatic injuries to face and teeth are more common in patients with epilepsy. It is essential that dentists should be well versed with the side effects related to all AEDs, particularly belonging to the newer generation. It is necessary to provide prophylactic management to prevent oral trauma.

Key words: Anti-epileptic drugs, Epilepsy, Gingival hyperplasia, Oral trauma, Seizures

Access this article online

www.ijss-sn.com

Month of Submission : 03-2020
Month of Peer Review : 04-2020
Month of Acceptance : 05-2020
Month of Publishing : 05-2020

INTRODUCTION

The overall prevalence of epilepsy in general population is 0.9%. Epilepsy is a chronic disorder of brain with unpredictably recurring seizures. According to International League Against Epilepsy, epilepsy is diagnosed when a person has two or more unprovoked seizures.[1] A seizure is

Corresponding Author: Dr. Nanika Mahajan, Department of Pedodontics and Preventive Dentistry, Indira Gandhi Government Dental College, Jammu, Jammu and Kashmir, India.

classified as "partial" when the electric discharge causing it occurs in a specific area of the brain or "generalized" when the discharge affects the entire brain cortex. When there is loss of awareness, seizures are termed complex [Table 1]. The classification of epilepsy is similar. Epilepsy can be partial or generalized. When the specific etiology is not known for certain, these cases are defined as idiopathic or primary epilepsy. When the etiology of seizures is known, the condition is known as secondary or acquired epilepsy.[2,3]

The first episode of seizure usually requires the need for diagnosis. The physician must rule out whether the seizure is in fact a real seizure or some other condition. The other conditions included in the differential diagnosis are syncope, migraine headaches, strokes, or transient ischemic attacks and non-epileptic events (or pseudoseizures), seen in association with such psychiatric conditions as conversion disorder, anxiety, and depression. There are three primary steps in the diagnosis of epilepsy: Health history taking, neurological examination, and laboratory testing. Depending on the history and examination findings, laboratory work may be ordered. This may include blood tests and special diagnostic tests such as electroencephalogram, computed tomography, magnetic resonance imaging, positron emission tomography, neuro sonography, and lumber puncture.[2]

Table 1: Simplified version of the classification of seizures according to the International League Against Epilepsy[1]

Partial seizures
Simple partial seizures (awareness not impaired) • with minor signs (focal motor, versive, phonatory) • with somatosensory or special-sensory symptoms (somatosensory, visual, auditory, olfactory, gustatory) • with autonomic symptoms • with psychic symptoms (déjà vu, illusions, hallucinations)
Complex partial seizures • with simple partial onset followed by impairment of awareness • with impairment of awareness at onset
Partial seizures evolving to secondarily generalized seizures • simple partial seizures evolving to generalized seizures • complex partial seizures evolving to generalized seizures • simple partial seizures evolving to complex partial and then to generalized seizures
Generalized seizures
Absence seizures Myoclonic seizures Clonic seizures Tonic seizures Tonic–clonic seizures Atonic seizures
Unclassified seizures

The main treatment options for epileptic patients are anti-epileptic drugs (AEDs), surgical treatments or vagus nerve stimulation. The type and severity of the disorder decides the treatment option to be chosen. If the seizures cannot be controlled by the medications, surgical interventions are considered.[3] However, despite successful surgical treatments, most patients remain on AEDs. More than 15 AEDs have been approved for the epileptic treatment by America and Europe.[4]

Earlier, a single AED was administered to manage the disorder but today, a combined regimen is being used to ensure better results. The classical AEDs include phenytoin (PHT), phenobarbital (Pb), sodium valproate (VPA), carbamazepine (CBZ), ethosuximide, and the diazepam family.

Most of the literature stresses on the AEDs and its effects on tooth supporting structures. The epileptic patients often become dental patients, as these patients are more prone to oral health problems. The reasons for that are particularly xerostomia, and gingival hyperplasia related to AEDs (PHT, Pb, and CBZ) administration. These drugs alter the metabolism and increase the removal of Vitamin D from the body, contributing to osteopenia and osteomalacia, which predispose individuals to teeth and adjacent soft-tissue injuries.[5,6] Current recommendations for the pharmacological antiepileptic treatment in Poland do not include the use of PHT as a drug of choice.[7-9] A different situation is in India, the United States, and the United Kingdom where it is usually recommended.[10-12]

Children who experience seizures are prone to traumatic injuries within the facial skeleton.[13-16] Hence, the study was carried out to evaluate the oral side effects of AEDs, the seizure related injuries of the oral cavity and also, the associated dental treatment needs.[17-20]

MATERIALS AND METHODS

A cross-sectional comparative study was carried out on 600 consecutive epileptic patients visiting the outpatient department of the Department of Pedodontics and Preventive Dentistry of a tertiary care, Government Medical College in Jammu city from March 2019 to February 2020.

Inclusion Criteria

Children aged (5–14 years) diagnosed with epilepsy according to the definition of epilepsy given by the Commission on Epidemiology and Prognosis, International League Against Epilepsy and were under anti-epileptic medication for at least 1 year (as per patients' case records) before the day of dental examination.

Exclusion Criteria

The following patients were excluded from the study: Patients who

1. Were currently not taking any medication
2. Had started the medication less than a year
3. Had only febrile seizures or only neonatal seizures
4. Were on other medications known to cause gingival overgrowth.

A comparative study was conducted between 300 epileptic children and a control group of 300 which was formed from non-epileptic patients.

The oral examination was carried out by a single dentist (S.S.Y) to limit intra-examiner variability. The oral examination was carried out to assess the various oral side effects of AEDs and oro-dental traumatic injuries. The oral side effects included xerostomia, gingival hypoplasia, gingivitis, and glossitis. The intra-oral traumatic injuries which were taken into consideration were lip, cheek and tongue injuries, tooth fracture, temporomandibular joint (TMJ) injuries, nose fracture, eye – socket trauma, and skull crack.

The two groups were compared with regard to side effects of AEDs and oro-dental injuries. For statistical analysis, Pearson's Chi-square test was used to evaluate the correlation between the two groups.

Informed and written consent was taken from parents/guardians in English/local language (Urdu) before the examination.

RESULTS

The cause of epilepsy in most of the patients with epilepsy in the present study was unknown. The AEDs assessed were PHT, CBZ, Pb, and VPA. Mono AED drug therapy was mostly prescribed by the physicians, a few were on dual therapy [Figure 1]. Rarely three or four drug regimen was prescribed.

The common oral side effects of AED drugs seen were xerostomia, gingivitis, gingival hypoplasia, and glossitis [Table 2].

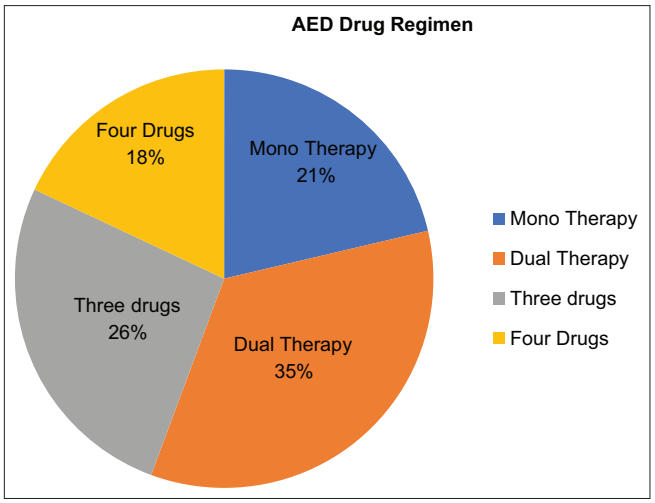

Figure 1: AED drug regimen used by patients

Table 2: Oral side effects seen in epileptic children on AED

Oral side effect of AED	*n*	%
Gingivitis	115	38.3
Gingival hyperplasia	99	33
Xerostomia	138	46
Glossitis	83	26.7

AED: Anti-epileptic drugs

Statistical Analysis

Chi-square

The Chi-square statistic is used to show whether or not there is a relationship between two variables.

This is the Chi-square equation:

$$\chi^2 = \sum_{i=1}^{n} \frac{(O_i - E_i)^2}{E_i}$$

Here,
χ^2=the Chi-square statistic
O_i=the observed frequency
E_i=the expected frequency
i=the number of the cell (cell 1, cell 2, etc.)
χ^2 value = 111.67 with degree of freedom=7.

Looking at our Chi-square table, we see that the critical Chi-square value for 7 degrees of freedom at the 0.001 probability level is 24.322. Since our calculated Chi-square value is greater than the critical Chi-square value, our results are significant at the 0.001 probability level.

We can also see that our results are also significant at the 0.01 as well as 0.05 probability levels. Therefore, there is a statistically significant relationship between traumatic

injuries between epileptic and non-epileptic patients using either 0.001 or 0.01 as our standard.

Pearson's correlation

The Pearson's correlation for traumatic injuries between epileptic and non-epileptic patients observed is 0.29 [Table 3]. The correlation between any two variables using Pearson's correlation will always be between –1 and +1.

The equation for Pearson's r is as follows:

$$r = \frac{\sum_{xy} - N\bar{x}\bar{y}}{\sqrt{(\sum x^2 - N\bar{x}^2)(\sum y^2 - N\bar{y}^2}}$$

This equation requires us to first calculate the sum of the product of all our data pairs, the means of both variables, and the sum of the squared values of both variables.

The value observed for our date is 0.29 which is very low. This indicates inadequate correlation for the traumatic injuries between epileptic and non-epileptic patients.

Hence, we can infer from both Pearson Chi-square test and correlation test that the traumatic injuries between epileptic and non-epileptic patients are highly independent of each other [Figure 2].

DISCUSSION

Most of the epileptic patients can be treated successfully with AEDs [Table 4]. Rarely, neurosurgery or vagus nerve stimulation is needed.[21,22] 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.[23] To control their seizures polydrug therapy is often indicated: ≤50%, attain control with one drug therapy; two drugs are required only in 10% cases, whereas 5% epileptic patients respond to three or four combinations of drug.[24] The quality of life of epileptic children gets affected due to deterioration in their oral health along with systemic and social problems.

The study done by Lundström *et al.* demonstrated that children and adolescents who took PHT develop larger number of gingival units with increase in depth of probing than individuals given CBZ during comparable period.[25] Findings in our study support previous reports that gingival enlargement seen in children on PHT medication is linked with the deposition of plaque in dentogingival areas with simultaneous inflammation of gingiva.[26,27] Non-modifiable factors such as genetic factor, age, and sex can predict individual's inherent risks for gingival hyperplasia.[26,28]

Table 3: Traumatic injuries in epileptic and non-epileptic patients

Traumatic injuries					
Injuries	**Epileptic patients**		**Non-epileptic patients**		
	n	**(%)**	***n***	**(%)**	**Total**
Lip or cheek bite	86	28.7	94	31.3	180
Tongue injuries	99	33	6	2	105
Tooth crack	111	37	42	14	153
Tooth fracture	76	25.3	124	41.3	200
Nose fracture	69	23	12	4	81
TMJ injuries	71	23.7	75	25	146
Eye socket trauma	49	16.3	5	1.7	54
Skull crack	32	10.7	3	1	35
Total	593		361		954

TMJ: Temporomandibular joint

Table 4: AED drug regimen consumed by patients

AED drug regimen	*n*	%
Mono therapy	64	21.3
Dual therapy	103	34.3
Three drugs	79	26.3
Four drugs	54	18

AED: Anti-epileptic drugs

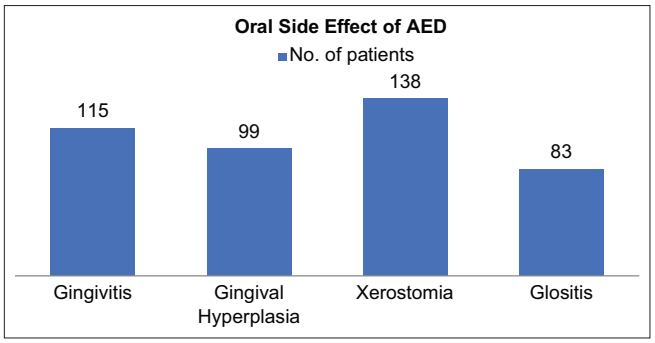

Figure 2: Oral side effects seen in epileptic children on AEDs

Gingival hyperplasia is characterized by the overgrowth of gingival subepithelial connective tissue and epithelium that develops about 1–3 months after the start of PHT treatment. This tissue enlargement typically begins at the interdental papilla and encroaches on the crowns of all teeth. Gingival overgrowth is not painful; however, gingival tissues that are traumatized during mastication, for example, may become tender. Growth hormone (GH) also creates conditions that allow plaque to accumulate easily, which increases bleeding in the dental sulcus and interdental papillary tissues. These factors make it much more difficult for patients to practice proper oral hygiene, resulting in the deterioration of their oral health. If left untreated, GH can shift the patient's dentition or cover the entire crown of the affected teeth.[29,30]

After numerous studies of the incidence of gingival hyperplasia in different populations treated with PHT,[31-35]

it is widely accepted that patients treated with PHT may experience gingival hyperplasia.

It is generally accepted that AEDs have side effects that diminish the patient's oral health; however, when the drugs are used short-term, such effects can be reversed, once treatment has ceased.[36] For patients taking AEDs for prolonged periods of time, good oral hygiene may be crucial to their ability to control the severity of GH. The role of the oral health-care professionals is critical in reducing the severity and extent of GH in patients on short-term or prolonged AED therapy. Patients need to attend educational sessions and prevention programs to motivate them to use proper oral hygiene, in addition to their regular visits to the dentist or dental hygienist. Such action should considerably diminish the side effects of AEDs therapy, such as GH.

The newer AEDs produce oral manifestations only infrequently. Xerostomia and stomatitis have been reported rarely as side effects of CBZ,[37] and rash that may involve the oral cavity has been associated with lamotrigine and can be exacerbated by the concomitant use of valproic acid.[38]

Valproic acid can cause direct bone marrow suppression, which can impair wound healing and increase post-operative bleeding and infections. Decreased platelet count is the most common and best-recognized hematologic effect of valproic acid; the incidence varies from 5% to 40%. Clinically, significant bleeding is uncommon because the thrombocytopenia is usually not severe. For elective surgery, laboratory evaluation — including bleeding time, fibrinogen level, prothrombin time, partial thromboplastin time, and von Willebrand factor level — is needed to assess the risk of peri- and post-operative bleeding. Bleeding as a potential side effect should be discussed with patients and their families in preparation for surgery.[39]

A number of drugs prescribed by dentists can jeopardize seizure control because they interact with AEDs. For instance, metronidazole, antifungal agents (such as fluconazole), and antibiotics (such as erythromycin) may interfere with the metabolism of certain AEDs.[40]

The co-administration of fluconazole and PHT is associated with a clinically significant increase in PHT plasma concentration, and the dose of the latter may require adjustment to maintain safe therapeutic concentrations. Other anticonvulsants, such as vigabatrin, lamotrigine, levetiracetam, oxcarbazepine and gabapentin, are unlikely to interact with fluconazole.

Clarithromycin increases the plasma concentration of CBZ, and co-administration of these drugs should be monitored very carefully to avoid CBZ toxicity.[41]

Valproic acid may be displaced from plasma proteins and metabolic pathways may be inhibited by high doses of aspirin; this interaction will free serum VPA concentrations resulting in subsequent toxicity.[42]

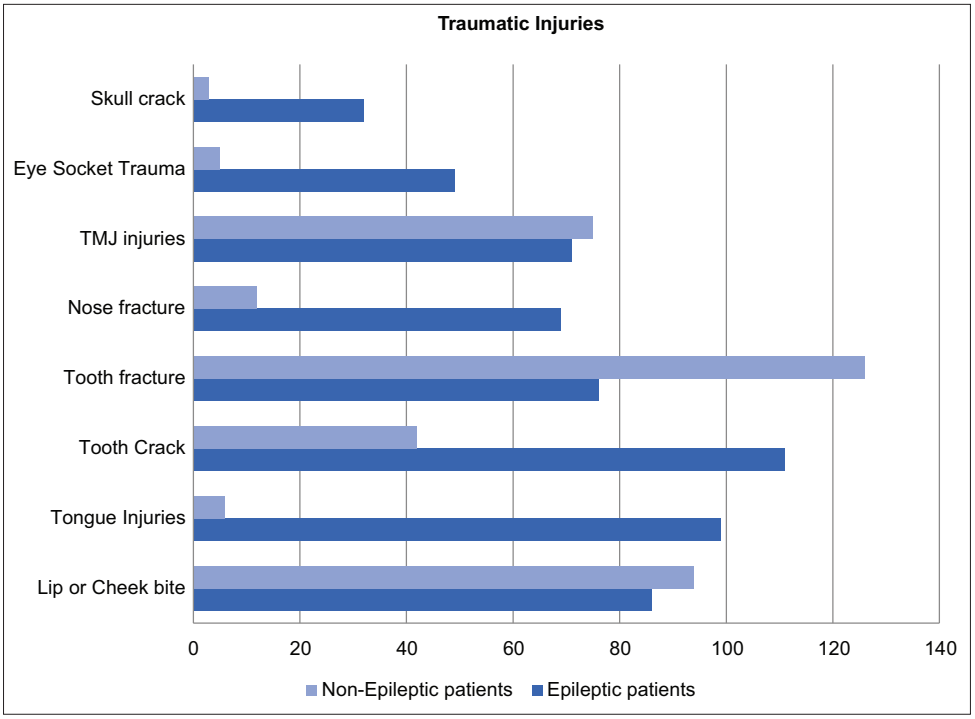

Figure 3: Traumatic injuries in epileptic and non-epileptic patients

The results showed that the patients with epilepsy were significantly more susceptible to facial and dental injuries than were the controls [Figure 3]. This has been reported by several other authors, including Martin, who stated that epileptic attacks can put patients at risk of suffering orofacial trauma.

According to Aragon and Burneo, the most common types of injuries that follow seizures are head trauma, fractures, and dental trauma.

The main aim of the scientists, as have been shown in a few publications, is focused on prevention of traumatic injuries in patients with epilepsy.[43] Many methods are invented for the prevention of intraoral injuries. Individually designed intraoral mouth guards, similar to those used by athletes, may be a great solution.

Individual, flexible intraoral mouth guards used during different sport disciplines, not only contact and extreme ones, provide excellent retention, stabilization, and high capacity to absorb energy, thus preventing trauma and reducing potential of the energy transferred to the temporomandibular joint or the base of the skull. They are made of a biocompatible material of proper thickness (3–5 mm). Most of the athletes, who use them, do not report their negative impact on speech or breathing.[34]

CONCLUSION

Traumatic injuries to face and teeth are more common in patients with epilepsy. It is essential that dentists should be well versed with the side effects related to all AEDs, particularly belonging to the newer generation.

Epileptic patients have severely inadequate mouth hygiene, oral health, and dental conditions. This is explained by the fact that these patients receive insufficient dental care because they spend only a short time in the dentist's chair due to the risk of seizure. Furthermore, their dental condition is worsened by injuries and damage caused to both hard and soft tissues in the maxilla-facial region during seizures. Therefore, protective measures such as the use of chlorhexidine and fluoride, education regarding oral hygiene, regular dental check-ups, and educating children to avoid sugary foods and drinks are crucially important.

Due to high frequency of dental trauma in epileptic patients, it is necessary to implement prophylactic management to prevent hard and soft tissues injuries. It seems that custom- made mouth guards in patients anticipating an epileptic seizure can be a good standard manner to prevent trauma. It is also necessary to pay special attention to the expansion and improvement of dental care concerning epileptic patients.

People with epilepsy can be safely treated in a general dental practice. A thorough medical history should be taken and updated at each visit. Seizure history must be taken into account when planning treatment. Dentists with a comprehension of seizure disorders can provide an invaluable service to their patients, providing not only oral health but also maintaining and promoting the systemic health of these patients.

REFERENCES

1. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on classification and terminology of the international league against epilepsy. Epilepsia 2019;60:89-99.
2. Turner MD, Glickman RS. Epilepsy in the oral and maxillofacial patient: Current therapy. J Oral Maxillofac Surg 2005;63:996-1005.
3. Busschots GV, Milzman BI. Dental patients with neurologic and psychiatric concerns. Dent Clin North Am 1999;43:471-83.
4. Jacobsen PL, Eden O. Epilepsy and the dental management of the epileptic patient. J Contemp Dent Pract 2008;9:54-62.
5. Aragon CE, Burneo JG. Understanding the patient with epilepsy and seizures in the dental practice. J Can Dent Assoc 2007;73:71-6.
6. Joshi SR, Pendyala GS, Saraf V, Choudhari S, Mopagar V. A comprehensive oral and dental management of an epileptic and intellectually deteriorated adolescent. Dent Res J (Isfahan). 2013;10:562-7.
7. Owen H, Waddell-Smith I. Dental trauma associated with anaesthesia. Anaesth Intensive Care 2000;28:133-45.
8. Mattson RH, Gidal BE. Fractures, epilepsy, and antiepileptic drugs. Epilepsy Behav 2004;5:S36-40.
9. Ghafoor PA, Rafeeq M, Dubey A. Assessment of oral side effects of antiepileptic drugs and traumatic ORO-facial injuries encountered in epileptic children. J Int Oral Health 2014;6:126-8.
10. Fisher RS. Redefining epilepsy. Curr Opin Neurol 2015;28:130-5.
11. Newton CR, Garcia HH. Epilepsy in poor regions of the world. Lancet 2012;380:1193-2011.
12. Neligan A, Hauser WA, Sander JW. The epidemiology of the epilepsies. Handb Clin Neurol 2012;107:113-33.
13. Alving J, Beniczky S. Epileptic prodromes: Are they nonconvulsive status epilepticus? Seizure 2013;22:522-7.
14. Gawlak D, Mierzwińska-Nastalska E, Mańka-Malara K, Kamiński T. Comparison of usability properties of custom-made and standard self-adapted mouthguards. Dent Traumatol 2014;30:306-11.
15. Gawlak D, Mańka-Malara K, Łuniewska J, Hovhannisyan A, Stojak W, Stróżyńska A, *et al*. Prevention of traumatic injuries and dental treatment of epileptic patients. J Stomatol 2015;68:468-75.
16. Gawlak D, Mańka-Malara K, Kamiński T. Ocena użytkowania indywidualnych ochraniaczy jamy ustnej wykonanych technikąewtryskowątbadania wstępne. Dent Med Probl 2014;2:218-24.
17. de Kinderen RJ, Evers SM, Rinkens R, Postulart D, Vader CI, Majoie MH, *et al*. Side-effects of antiepileptic drugs: The economic burden. Seizure 2014;23:184-90.
18. Mehmet Y, Senem O, Sülün T, Hümeyra K. Management of epileptic patients in dentistry. Surg Sci 2012;3:47-52.
19. Behere PB, Marmarde A, Singam A. Dislocation of the unilateral temporomandibular joint a very rare presentation of epilepsy. Indian J Psychol Med 2010;32:59-60.
20. Gautam A, Verma PK, Srivastava R, Lodhi K. Esthetic correction of phenytoin induced gingival hyperplasia-case reports. Health Care 2013;1:28-31.
21. Akor F, Liu NM, Besag FM, Ahmed MA. Value of tongue biting in differentiating betweenepileptic seizures and syncope. Seizure 2013;22:328.
22. Singh NA, Khan M, Vijayalakshmi KR, Subhas GT, Nataraju B, Anitha M. Phenytoin, folic acid and gingival enlargement: Breaking myths. Contemp Clin Dent 2014;5:59-66.
23. International League against Epilepsy, International AED Database; 2010. Available from: http://www.aesnet.org/go/practice/aedinfo. [Last accessed

on 2017 Feb 25].
24. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342:314-9.
25. Lundström A, Eeg-Olofsson O, Hamp SE. Effects of anti-epileptic drug treatment with carbamazepine or phenytoin on the oral state of children and adolescents. J Clin Periodontol 1982;9:482-8.
26. Nuki K, Cooper SH. The role of inflammation in the pathogenesis of gingival enlargement during the administration of diphenylhydantoin sodium in cats. J Periodontal Res 1972;7:102-10.
27. Donnenfeld OW, Stanley HR, Bagdonoff L. A nine month clinical and histological study of patients on diphenylhydantoin following gingivectomy. J Periodontol 1974;45:547-57.
28. Hassell TM. Epilepsy and the oral manifestations of phenytoin therapy. In: Myers H, editor. Monographs in Oral Science. Basel: S. Karger; 1981.
29. Angelopoulos AP, Goaz PW. Incidence of diphenylhydantoin gingival hyperplasia. Oral Surg Oral Med Oral Pathol 1972;34:898-906.
30. Angelopoulos AP. A clinicopathological review. Diphenylhydantoin gingival hyperplasia: 2. Aetiology, pathogenesis, differential diagnosis and treatment. Dent J 1975;41:275-7, 283.
31. Klar LA. Gingival hyperplasia during dilantin-therapy; a survey of 312 patients. J Public Health Dent 1973;33:180-5.
32. Seymour RA, Smith DG, Turnbull DN. The effects of phenytoin and sodium valproate on the periodontal health of adult epileptic patients. J Clin Periodontol 1985;12:413-9.
33. Thomason JM, Seymour RA, Rawlins MD. Incidence and severity of phenytoin-induced gingival overgrowth in epileptic patients in general medical practice. Community Dent Oral Epidemiol 1992;20:288-91.
34. Prasad VN, Chawla HS, Goyal A, Gauba K, Singhi P. Incidence of phenytoin induced gingival overgrowth in epileptic children: A six month evaluation. J Indian Soc Pedod Prev Dent 2002;20:73-80.
35. Prasad VN, Chawla HS, Goyal A, Gauba K, Singhi P. Folic acid and phenytoin induced gingival overgrowth-is there a preventive effect? J Indian Soc Pedod Prev Dent 2004;22:82-91.
36. Dahllöf G, Axiö E, Modéer T. Regression of phenytoin-induced gingival overgrowth after withdrawal of medication. Swed Dent J 1991;15:139-43.
37. Ogunbodede EO, Adamolekun B, Akintomide AO. Oral health and dental treatment needs in Nigerian patients with epilepsy. Epilepsia 1998;39:590-4.
38. Li LM, Russo M, O'Donoghu MF, Duncan JS, Sander JW. Allergic skin rash with lamotrigine and concomitant valproate therapy: Evidence for an increased risk. Arq Neuropsiquiatr 1996;54:47-9.
39. Archarya S, Bussel JB. Hematologic toxicity of sodium valproate. Pediatr Hematol Oncol 2000;22:62-5.
40. Goulden KJ, Dooley JM, Camfield PR, Fraser AD. Clinical valproate toxicity induced by acetylsalicylic acid. Neurology 1987;37:1392-4.
41. Patsalos PN, Frosher W, Pisani F, van Rijn CM. The importance of drug interactions in epilepsy therapy. Epilepsia 2002;43:365-85.
42. Miners JO. Drug interactions involving aspirin (acetylsalicylic acid) and salicylic acid. Clin Pharmacokinet 1989;17:327-44.
43. Adewole RA, Ojini FI, Akinwande JA, Danesi MA. Oro-dental and maxillofacial trauma in epilepsy at a Tertiary hospital in Lagos. West Afr J Med 2011;30:114-7.

How to cite this article: Mahajan N, Mahajan P, Khajuria A, Kotwal B, Kaul B, Gupta R. Role of Cumulative Anti-epileptic Drug Load on the Periodontal Health Tissues and Seizure Related Traumatic Oro-dental Injuries - A Comparative Cross-sectional Study in a Tertiary Health Institution in Jammu City. Int J Sci Stud 2020;8(2):78-84.

Source of Support: Nil, **Conflicts of Interest:** None declared.