Evaluation of oral health status in patients receiving antiepileptic medications

Farqad Najm Abed, B.D.S. [(1)]
Raja H. Al –Jubouri, B.D.S., M.Sc., Ph.D. [(2)]

ABSTRACT

Background: Epilepsy is a common neurological disorder of incidence rate 1-2%. Genetic, congenital, developmental, tumors, head trauma and central nervous system infections maybe the cause of epilepsy. This study aimed to determine the prevalence of stomatitis, xerostomia and taste disorder among patients taking carbamazepine or sodium valproate and to make salivary analysis for IgA, cystatin c and salivary flow rate.

Material and method:This study performed in al- Yarmuk teaching hospital in Baghdad, Samples consist of (70) epileptics half of them treated with carbamazepine and other half treated with sodium valproate, and (18) healthy control group of both genders and with different ages to detect the prevalence of oral manifestations, salivary IgA and cystatin C changes.

Results: Salivary IgA is significantly higher in epileptics than healthy group. DMFT is significantly lower in epileptics than in healthy control. GI is hardly affected by epilepsy. Salivary flow rate was significantly lower in epileptics than the healthy control group. On the other hand, cystatin C was obviously higher in epileptics but failed to reach the level of statistical significance. Mucositis in epileptics was significantly higher. Candidal infection and Dysguisia failed to reach the level of statistical difference.

Conclusion: The most affected oral measurement by epilepsy was salivary IgA then salivary flow rate followed by DMFT. Cystatin C had a marginal contribution to the context of case –control discrimination.Sodium valproate is safer than carbamazepine when compared by its effects on the oral health. Mucositis, candida infection and dysguisia were lower in epileptics who were treated with Sodium valproate. Salivary flow rate was higher in Sodium valproate - treated group than in carbamazepine group. GI and DMFT were lower in sodium valproate treated group than the carbamazepine group.

Keyword: Salivary IgA, cystatin C, antiepileptic medications (AEMs). (J Bagh Coll Dentistry 2014; 26(2): 69-73).

الخلاصة:

الصرع اضطراب عصبي شائع معدل الاصابة1-2%. الأورام الوراثية والخلقية والتنموية، الصدمات النفسية والتهابات الجهاز العصبي المركزي هي من اهم اسباب الصرع.

هدف دراسة: لتحديد مدى انتشار اضطراب التهاب الفم، وجفاف الفم، والذوق بين المرضى الذين يتناولون كاربامازبين أو الصوديوم فالبرويت وتحليل اميونو غلوبيولين أ، سيستاتين ج ومعدل تدفق اللعاب .

المواد والطريقة: هذه الدراسة أجريت في مستشفى اليرموك في بغداد، تتكون العينات من (70) مريض مصاب بالصرع يتم علاج نصفهم مع كاربامازبين، والنصف الآخر مع فالبرويت الصوديوم، وفريق مراقبة صحية (18) من كلا الجنسين ومع الإعمار المختلفة للكشف عن انتشار التغييرات الشفوية، اميونو غلوبين

النتائج: اميونو غلوبيولين أ أعلى بكثير في الصرع من مجموعة المراقبة. مقياس التسوس أقل بكثير في الصرع مما في مجموعة المراقبة. مقياس التهاب اللثة لا يكاد يتأثر بالصرع. وكان معدل تدفق اللعاب أقل بكثير في الصرع من مجموعة المراقبة الصحية. في حين ان السيستاتين ج كان أعلى في الصرع ولكنه فشل في الوصول إلى مستوى الدلالة الإحصائية. التهاب الغشاء المخاطي في الصرع كان أعلى بكثير. الإصابة بالفطريات وتغييرات التذوق فشلتا في التوصل إلى مستوى الفرق الإحصائي.

الاستنتاج: المقساس الشفوي الأكثر تأثرا بالصرع كان الاميونوغلوبيولين أ ثم معدل تدفق اللعاب تليها مقياس التسوس. وكان سيستاتين ج ذو مساهمة هامشية في سياق التمييزبين المصابين والاصحاء. فالبرويت الصوديوم أكثر أماناً من كاربامازبين إذا ما قورنت بإثارة على صحة الفم والأسنان. التهاب الغشاء المخاطي والفطريات واضطرابات التذوق كانتأقلفيالصرعالذينيتم علاجهمبفالبرويتالصوديوم. وكانمعدلتدفقاللعابأعلىفيمجموعة فالبرويتالصوديوممافيمجموعةكاربامازبين. مقياس التهاب اللثه ومقياس التسوسكانتأقلفيمجموعة فالبرويتالصوديوم مما هي عليه في مجموعةالكاربامازبين.

مفاتيح البحث :اميونوغلوبيولين أ,سيستاتين ج, الادوية المضادة للصرع.

INTRODUCTION

Epilepsy is defined as a neurological condition characterized by recurrent epileptic seizures unprovoked by any immediately identifiable cause. An epileptic seizure is the clinical manifestation of an abnormal and excessive discharge of a set of neurons in the brain [(1)].

Epilepsy should be viewed as a symptom of an underlying neurological disorder and not as a single disease entity. The clinical presentation of epilepsy depends on a number of factors, chiefly: the parts of the brain affected the pattern of spread of epileptic discharges through the brain, the cause of the epilepsy and the age of the individual [(2)].

The classification of the epilepsies is controversial and has tended to focus on both the clinical presentation (type of epileptic seizure) and on the underlying neurological disorder [(3)].

Epilepsy is primarily a clinical diagnosis based on a detailed description of the events before, during and after a seizure given by the person and/or witness. Electroencephalogram (EEG), magnetic resonance imaging (MRI) and computed tomography (CT) are used to investigate individuals with known and suspected epilepsy [(4)].

The UK National General Practice Study of Epilepsy found that 60% of people with epilepsy have convulsive seizures, of which two thirds have focal epilepsies and secondarily generalized seizures and the other third have generalized tonic-clonic seizures. They also found that the majority (60%) of people with newly diagnosed or suspected epileptic seizures had epilepsy with no

(1) M.Sc. Student, Department of Oral Diagnosis, College of Dentistry, University of Baghdad.

(2) Professor, Department of Oral Diagnosis, College of Dentistry, University of Baghdad.

identifiable etiology. Vascular disease was the etiology in 15% and tumor in 6%. Among older subjects the proportion with an identifiable cause was much higher: 49% were due to vascular disease and 11% to tumors [5].

The mainstay of treatment for epilepsy is antiepileptic medications (AEMs) taken daily to prevent the recurrence of epileptic seizures. Since the development of MRI there has been an increase in the number of people identified with epilepsy who could benefit from surgery. There is also a need to ensure provision of appropriate information to people with epilepsy and their carries [6].

It is a general impression that patients with epilepsy tend to have poorer oral health and receive less adequate dental treatment in comparison with the general (nonepilepsy) population [7]. A survey of oral health and dental status of patients with epilepsy in comparison with the non-epilepsy population had been taken. Only one such survey has been published [8], which was, however, uncontrolled. Others concentrated on only the periodontal status in relation to antiepileptic medication (AEMs) [9].The aim was to test statistically whether these patients did indeed have poorer oral health compared with that of the nonepilepsy population, and if so, to cast light on the possible reasons and measures to be taken to avoid it. Oral health is an important aspect of quality of life, and every effort should therefore be made to improve oral health, especially in a group of people already disadvantageously affected by their disease.

Since no extensive study was conducted in Iraq on the effect of epilepsy and AEMs on the oral health (Carbamazepine and sodium valproate), therefore this study was to detect the relationship between epilepsy and oral health status in relation to salivary IgA, Cystatin C and salivary flow rate were determined.

MATERIALS AND METHODS

The study sample consisted of (70) patients complaining from epilepsy, 50 % of them (35) patients were taking carbamazepine; the other 50% (35) patients were taking sodium valproate (patients were on medication for minimal 6 months) and the control group is (18) apparently healthy individual of both genders; they were examined from the period (Jan-2013 to May -2013) in Al-Yarmouk Teaching Hospital in Baghdad, to detect the oral manifestations related to these antiepileptic medications and IgA and Cystatin C were measured in the saliva of both groups. Approval was obtained from Ministry of Health for patient's examination and collection of saliva and laboratory work.

Exclusion criteria:

Patients with other chronic diseases such as: metabolic, liver disease, severe inflammation, malignancy or children under the age of 6 or individuals above 60 years.

Instruments used for oral examination of patients

- Diagnostic instruments
- Disposable gloves.
- Periodontal probes.
- Antiseptic solution (Hipitane 5%).
- Dental Chair

Oral Examination

All the patients examined by a single examiner, under standardized conditions; the oral cavity examined by diagnostic instrument.

The procedure of examination of oral soft tissue was done in sequence according to directions suggested by the WHO(1987), the examination begun with the lip, upper and lower sulcus, retro-molar area, upper and lower labial mucosa, buccal mucosa, then the hard and soft palate, dorsal, margins and inferior surface of tongue, floor of the mouth were also examined.

In case of oral mucosal lesion, the duration, size, clinical description, location of lesion, and finally the clinical diagnosis were stated.

Oral Manifestations

Dry Mouth (Salivary flow rate)

Dry mouth is a common symptom most often caused by a decrease in the amount of saliva or a change in the quality of saliva. [10].

In this study dry mouth and salivary flow rate were diagnosed according to the anamenesis below: Does your mouth feel dry? Do you experience any difficulties in chewing dry foods? Do you experience any difficulties in swallowing dry foods? Are you aware of any recent increase in the frequency of liquid intake? [11]

Salivary flow rate measurement

The average salivary flow rate was obtained from the total volume collected in the study time [12] and salivary flow rate was calculated as ml/min.

Mucositis

Oral mucositis is inflammation of the mucosa of the mouth which ranges from redness to severe ulceration. Symptoms of mucositis vary from pain

and discomfort to an inability to tolerate food or fluids

Candidal infection

It was determined clinically.

Dysguisia

Taste alteration can be diagnosed in this study according to the criteria taken from the European Organization for Research and Treatment of Cancer (EORTC): Have you had problems with your sense of taste? and did food and drink taste different from usual? The abnormal taste may appear bizarre or limited to a part of the mouth. [13].

Caries presentation DMFT index [14] :

Decayed-Missing-Filled Index (DMF) which was introduced by Klein, Palmer and Knutson in 1938 and modified by WHO:

DMF teeth index (DMFT) which measures the prevalence of dental caries/Teeth.

Gingival overgrowth and bleeding(Gingival Index) [15].

Indices used for gingival disease assessment:

*Gingival Index (GI).... which was introduced by Loe and Silness in 1963

Immunological analysis

Saliva collection: the method of Wu-Wang was used for saliva collection [16]. To avoid circadian variation, saliva samples were collected between 9 a.m. and 1 p.m. In order to obtain a sample of total saliva, the patients were instructed not to eat or drink (except water) for 1 hour [17].

Mouth washing with pure water was carried out right before sampling. All participants were instructed to collect saliva in their mouths for 5 minutes and to spit into a clean plastic container (plain tube). Saliva samples were kept in ice during the collection. In order to reduce bubble and foam, samples were centrifuged, pipetted into two androff tubes one for IgA and the other for Cystatin C analysis and stored at 70 ^{o}C freezer until immunological analysis [18].

Finally levels of salivary IgA and Cystatin C were determined by ELISA.

Immunological analysis (Salivary IgA)

Determination of salivary IgA is done by Enzyme Link Immunosorbent Assay ELISA [19].

Immunological analysis (Cystatin C)

This assay employs the quantitative sandwich enzyme immunoassay technique. Antibody specific for Cys-C has been pre-coated onto a micro plate. Standards and samples are pipetted into the wells and any Cys-C present is bound by the immobilized antibody. After removing any unbound substances, a biotin-conjugated antibody specific for Cys-C is added to the wells.

After washing, avidin conjugated Horseradish Peroxidase (HRP) is added to the wells. Following a wash to remove any unbound avidin-enzyme reagent, a substrate solution is added to the wells and color develops in proportion to the amount of Cys-C bound in the initial step. The color development is stopped and the intensity of the color is measured.

RESULTS

The mean age range of sodium valproate group was significantly lower than carbamazepine group. As shown in Table 1.

Table 1: The difference between Carbamazepine and sodium valproate treatment for epilepsy on mean of age range

	Carbamazepine	sodium valproate	P
Age (years)			<0.001
Range	(6 - 60)	(6 - 60)	
Mean	31.5	20.4	
SD	13.9	11	
SE	2.36	1.87	
N	35	35	

Table 2: The difference between Carbamazepine and sodium valproate treatment for epilepsy on mean of salivary IgA, DMFT and GI.

	Carbamazepine	Sodium valproate	P
Salivary IgA			0.74[NS]
Range	(59 - 369)	(80 - 379)	
Mean	237.8	244.5	
SD	91.7	75.9	
SE	15.5	12.83	
N	35	35	
DMFT			0.02
Range	(1 - 20)	(0 - 20)	
Mean	7.9	5.5	
SD	3.9	4.4	
SE	0.65	0.74	
N	35	35	
Gingival Index			0.008
Range	(0.12 - 1.43)	(0.04 - 1.25)	
Mean	0.63	0.43	
SD	0.31	0.29	
SE	0.052	0.049	
N	35	35	

Both DMFT and GI were significantly lower in sodium valproate group than carbamazepine group. While IgA was higher in valproate group but failed to reach the statistical significance (Table 2).

Salivary flow rate was higher in sodium valproate group and cystatin C was lower in the same group than in carbamazepine group, even though both differences were not significant. (Table 3).

Table 3: The difference between Carbamazepine and sodium valproate treatment for epilepsy on median of salivary flow rate and Cystatin C.

	Carbamazepine	Sodium valproate	P
Salivary Flow Rate			0.2 [NS]
Range	(0.01 - 1.2)	(0.02 - 1.3)	
Median	0.2	0.33	
Inter-quartile range	(0.05 - 0.56)	(0.1 - 0.52)	
N	35	35	
Mean rank	32.4	38.6	
Salivary Cystatin C			0.51 [NS]
Range	(20.5 - 450)	(17 - 320)	
Median	80	72	
Inter-quartile range	(60 - 135)	(45 - 150)	
N	35	35	
Mean rank	37.1	33.9	

In figure (1) it is shown that mucositis was significantly higher in carbamazepine group than valproate group. Both candida infection and dysguisia were higher in carbamazepine group but fail to reach statistical significance.

DISCUSSION

Salivary IgA is the prominent immunoglobulin and is considered to be the main specific defense mechanism in oral cavity [8].

The variations in the immunoglobulin level in different studies are related to the source, method of collection, measurement as well as number of other variable, the salivary secretion rates may inversely influence the IgA concentration in saliva [20].

IgA was higher in valproate -group, this may be due to the effect of the drug on the immune system.

DMFT and GI were lower in valproate group as they have higher IgA

The present study shows that the mucositis is significantly lower in patient on sodium valproate treatment as compared to the carbamazepine group this may be due to higher salivary flow rate and higher IgA.

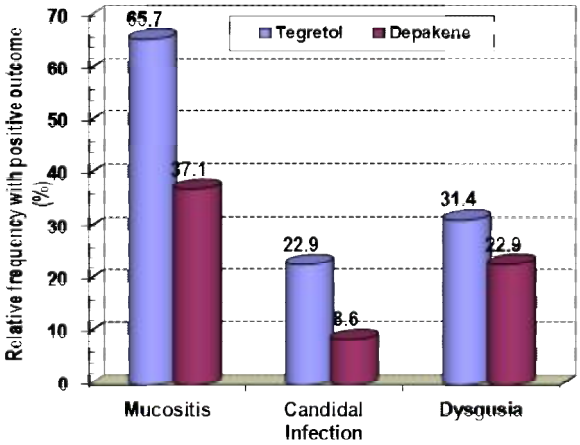

Figure 1: Bar chart showing Carbamazepine - sodium valproate difference in positivity rate of selected clinical features. Tegretol and depakene are the trade names for carbamazepine and sodium valproate respectively.

REFERENCES

1. Robert Fisher S, Leppik Ilo. When does a seizure imply epilepsy? J Epilepsia 2008; 49: 7–12.
2. Duncan JS, Shorvon SD, Fish DR. Clinical epilepsy. New York: Churchill Livingstone; 1995.
3. Jerome Engel Jr. ILAE classification of epilepsy syndromes. Epilepsy Res J 2006; 70: 5–10.
4. Engel Jr. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: Report of the ILAE task force on classification and terminology. Epilepsia 2001; 42(6): 796-803.
5. David McCandles W. Epilepsy: Epidemiology of epilepsy. Epilepsia 2012; 98: 29-40.
6. MacDonald BK, Johnson AL, Goodridge DM. Factors predicting prognosis of epilepsy after presentation with seizures. Ann Neurol 2000; 48(6): 833-41.
7. Shaw MJ, Shaw L, Foster TD. The oral health in different groups of adults with mental handicaps attending Birmingham (UK) adult training centers. Community Dent Health 1990; 7: 135–41.
8. Ogunbodede EO, Adamolekun B, Akintomide AO. Oral health and dental treatment needs in Nigerian patients with epilepsy. Epilepsia 1998; 39: 590–4.
9. Galas-Zgorzalewicz B, Borysewicz-Lewicka M, Zgorzalewicz M. The effect of chronic carbamazepine, valproic acid and phenytoin medication on the periodontal condition of epileptic children and adolescents. Funct Neurol 1996; 11:187-93.
10. Sankar V, Rhodus, N. The American Academy of Oral Medicine. Dry mouth (Xerostomia) 2007; 425: 778-6162.
11. Azambuja S, Henrique P, Jacobs R, Nackaerts O, Fischer IR, Henrique F, Jorge S, Aparecido S, Maitê

Barroso da, Lúcia A. Clinical diagnosis of hyposalivation in hospitalized patients. J Appl Oral Sci 2012; 20:157-61.
12. Thaweboon S, Thaweboon B, Nakornchai S, Jitmaitree S. Salivary secretory IgA, pH, flow Rates Mutans Streptococci and Candida in Children with rampant caries. Southeast Asian J Trop Med Public Health 2008; 39:893-9.
13. Cawson RA, Odell EW. Essentials of oral pathology and oral medicine. 8th ed. 2008. p.441.
14. Burt BA, Eklund SA. Dentistry, Dental Practice and the Community. 6th ed. Philadelphia: WB Saunders; 2005.
15. Worthington HV, Jan Clarkson EW, Bryan G, Paul BV. Routine scale and polish for periodontal health in adults. J Clin Periodontol 2013; 40:1016-24.
16. Wu-Wang CY, Patel M, Feng J, Milles M, Wang SL. Decreased levels of salivary prostaglandin E2 and epidermal growth factor in recurrent aphthous stomatitis. Arch Oral Biol 1995; 40:1093-8.
17. Martinez, KO, Mendes LL and Alves JB. Secretory a immunoglobulin, total proteins and salivary flow in recurrent aphthous ulceration. Rev Bras Otorrinolaringol 2007; 73: 323-8.
18. Externest DB, Meckelein MA, Schmidt FA. Correlations between antibody immune responses at different mucosal effectors sites are controlled by antigen type and dosage. Elsevier Sci 2000; 68: 3830-9.
19. Valdimarsdottir HB, Arthur A. Stone-psychosocial factors and secretory IgA. Critical Reviews in Oral Biology & Medicine 1997; 8:461-474.
20. Eliasson L, Birkhed D, Osterberg T, Carlén A. Minor salivary gland secretion rates and immunoglobulin A in adults and the elderly. Eur J Oral Sci 2006 114(6): 494-9.