ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

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RADIOLOGICAL ASSESSMENT OF THE PREVALENCE AND LOCATION OF ROOT RESORPTION IN EPILEPTIC PATIENTS: AN OBSERVATIONAL STUDY

EPİLEPSİ HASTALARINDA KÖK REZORPSİYON PREVALANSININ VE LOKASYONUNUN RADYOLOJİK DEĞERLENDİRMESİ–GÖZLEMSEL BİR ÇALIŞMA

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Öz

Amaç

Epilepsi hastalarının tedavisinde kullanılan antiepileptik ilaçlar kemik dokusu üzerinde olumsuz etki yapmaktadır ancak bildiğimiz kadarı ile bu hastalarda diş kökü rezorpsiyonu araştırılmamıştır. Bu çalışmanın amacı, antiepileptik ilaç kullanan epilepsi hastalarında eksternal ve internal kök rezorpsiyon prevalansını ve rezorpsiyon bölgelerine göre dağılımını değerlendirmektir.

Gereç ve Yöntem

Diş tedavisi öncesi elde edilen panoramik radyografiler değerlendirildi. Vaka grubu sadece epilepsili bireylerden oluşurken, kontrol grubu sağlıklı bireylerden oluştu. Tüm dişlerde (üçüncü azı dişleri hariç) dış ve iç rezorpsiyon varlığı/yokluğu, rezorpsiyon bölgesi (kökün servikal, orta ve apikal bölgesi), yaşı ve cinsiyeti bir excel dosyasına kaydedildi. Dağılımın normalliğine göre bağımsız örneklem t-testi veya Mann-Whitney U testi ve kategorik değişkenleri karşılaştırmak için ki-kare testi kullanıldı.

Bulgular

424 hastanın (236 sağlıklı birey ve 188 epileptik hasta) 93'ünde (%21,9) rezorpsiyon olduğunu gösterse de gruplar arasında eksternal ve internal rezorpsiyon varlığı açısından anlamlı farklılık yoktu (p = 0,089 ve 0,746). Rezorpsiyon 30 yaş üstü ve erkeklerde daha sıktı (p=0,018 ve 0,013).

Sonuç

Epilepsi hastalarında rezorpsiyon varlığının sağlıklı deneklerden farklı olmadığı sonucuna vardık. Ancak epilepsili hastalarda rezorpsiyon en çok alt azı dişleri ve orta 1/3 bölgede görüldü. Klinisyenler bu hastalarda diş tedavisi yaparken sonuçlarımızı dikkate almalıdır.

Anahtar Kelimeler: Antiepileptik İlaç, Epilepsi, Panoramik Radyografi, Rezorpsiyon

Abstract

Objective

Antiepileptic drugs used in the treatment of epilepsy patients have a negative effect on bone tissue, but

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as far as we know, tooth root resorption has not been investigated in these patients. The aim of this study was to evaluate the prevalence of external and internal root resorption and its distribution according to resorption sites in epilepsy patients using antiepileptic drugs.

Material and Method
Panoramic radiographs obtained before dental treatment were evaluated. While the case group consisted of only those with epilepsy, the control group included healthy subjects. The presence/absence of external and internal resorption of all teeth (except the third molars), region of resorption (cervical, middle, and apical region of the root), age, and sex were recorded in an excel file. Independent sample t-test or Mann-Whitney U test according to normality of distribution and a chi-square test to compare categorical variables were used.

Results
The resorption in 93 (21.9%) of 424 patients (236 healthy subjects and 188 epileptic patients), the groups did not significantly differ by the presence of external and internal resorption (p = 0.089 and 0.746). It was more common in those over 30 years and males (p = 0.018 and 0.013).

Conclusion
We concluded that the presence of resorption in epilepsy patients was not different from healthy subjects. However, in patients with epilepsy, resorption was mostly seen in the lower molars and middle 1/3 regions. Clinicians should consider our results when treating these patients.

Keywords: Antiepileptic Drug, Epilepsy, Panoramic Radiography, Resorption

Introduction

Epilepsy is known to be the most prevalent neurological disorder affecting about 50 million people worldwide (1). The mainstay of the treatment is medical therapies with antiepileptic drugs (AEDs) (2). Among the greatest concerns with the use of AEDs is that significant metabolic effects may appear on bone years later, as the disorder requires prolonged drug therapy. AED drugs are very diverse. New AEDs such as levetiracetam, oxcarbazepine, lamotrigine, and classic AEDs such as carbamazepine, phenytoin (3,4). Although the mechanism of action of AEDs on bone is not clear, it is reported that AEDs that induce CYP450 by inducing Cytochrome p450 enzyme (classical AED phenobarbital, carbamazepine) cause bone loss by negatively affecting vitamin D metabolism (4). Other possible mechanisms include calcitonin deficiency, hyperhomocysteinemia, vitamin K and carnitine deficiency, sex hormone deficiency and direct action on osteoclasts (5). On the other hand, it has been shown that AED reduces dentin tissue as well as bone tissue in rats with continued growth (6). The literature hosts studies comparing the oral and dental health of epileptic patients with the general population. For example, previous research highlighted that epileptic patients have worse oral health and receive more inadequate dental treatment compared to the general population (7, 8). Moreover, some other studies compared periodontal, caries, and oral hygiene statuses between the two groups (7, 9-11).

Resorption is a condition associated with a physiological or pathological process resulting in the loss of dentin, cementum, and/or bone (12). The mineralized tissues of permanent teeth are generally not resorbed, but the etiology of root resorption occurs with the injury of non-mineralized tissues covering the outer surface of the root (precementum) or the inner surface of the root canal (predentin) (13, 14). The continuation of the resorption depends highly on common stimulation factors of osteoclastic cells, such as infection or pressure (15). The etiology and pathogenesis of tooth root resorption have not been fully elucidated yet, but the most prominent etiological factors are known to be trauma, pulp infection, tooth whitening, and orthodontic treatment. Root resorption is primarily asymptomatic; therefore, it occurs incidentally on radiographic examination (16). Knowing the etiological and risk factors of root resorption and performing regular radiographic examinations when necessary may make it possible to detect resorption at an early stage and prevent its further development. In 2009, Patel, Kanagasingam and Ford (17) divided root resorption into internal and external (superficial, inflammatory, replacement, cervical, and apical temporary) by its localization on the root surface. While root resorption can be diagnosed using periapical radiography (18), digital panoramic radiography (19), or cone beam computed tomography (CBCT) (20), panoramic radiography is considered a more useful tool for detecting root resorption (21) and is highly recommended as a complementary examination in many countries such as Korea (22), Sweden (23), and Belgium (24). Thus, the chance of detecting root resorption first is relatively high on a panoramic radiograph.

Epidemiological research may provide valuable insights into trends and risk factors in the incidence and prevalence of diseases. The relevant data are deemed helpful in planning healthcare strategies to prevent or alleviate emerging conditions (6). The literature hosts a plethora of epidemiological studies investigating the prevalence of root resorption (25-27). In general, it is assumed that one may discover a similar prevalence and distribution of root resorption among different tooth groups in the general population of the same socioeconomic status. Since oral health is considered key to attaining a substantial quality of life, uncovering root resorption seems important to improve the oral health of individuals with specific disorders such as epilepsy. There are not enough studies on root resorption and systemic disease and drug use (28-31). However, the research interest seems to have missed evaluating the prevalence and localization of root resorption among epileptic patients. Considering that epilepsy patients frequently apply to dental clinics for dental treatment, there is a need for a study on this subject.

The null hypothesis of this study is that the incidence, location and type of root resorption are not different from the healthy group. Therefore, the present study aimed to retrospectively reveal the prevalence of external and internal root resorption types and the distribution of resorptions by cervical, middle, and apical regions of the root among epileptic patients on their panoramic radiographs.

Material and Methods

Ethical approval of the study was given by the ethics committee of Necmettin Erbakan University, Faculty of Dentistry, Pharmaceutical and Non-Medical Non-device research. (Decision no: 2022-251). This study was conducted in accordance with all versions of the Declaration of Helsinki.

Panoramic radiographs of the patients taken during the first examination in the Department of Oral Diagnosis and Radiology at Necmettin Erbakan University, Faculty of Dentistry, were retrospectively analyzed. Information about the systemic anamnesis and medications of the patients was obtained from the digital patient management system. Panoramic radiographs of good diagnostic quality, randomly selected from systemically healthy patients, were included in the study. Only randomly selected panoramic radiographs from patients with epilepsy and regular use of antiepileptic drugs were included. From these radiographs, radiographs of patients aged 18-45 years were selected. The study also included people with no missing teeth except the 3rd molar on radiographs. Patients with a history of orthodontic treatment, tooth whitening or trauma were also excluded.

The data (the presence/absence of external and internal resorption of all teeth (except the third molars), region of resorption (cervical, middle, and apical regions of the root), age, and sex) were recorded in an excel file. Each root of the multi-rooted teeth seen on the radiograph was evaluated. When resorption was detected in any root observed on the radiograph, resorption was considered as existing. An endodontist and an oral and maxillofacial radiologist with at least ten years of experience independently and blindly reviewed all digital images. For intraobserver and interobserver agreement, the observers evaluated 50 panoramic images twice in a one-month interval.

Power Analysis

The effect size was calculated based on data from the study by MARINESCU, BĂNICĂ, MERCUŢ, GHEORGHE, DRĂGHICI, COJOCARU, SCRIECIU and POPESCU (31) using G Power 3.0.10 (University Kiel, Germany) program. Accordingly, the expected value in the p(H0) hypothesis was set to 0.5-0.5, and the values 0.108-0.892 were entered as the p(H1) data. Therefore, we obtained an effect size of 0.784 and found at least 30 samples sufficient with a Type 1 error of 0.05 and a power of 99%. Although a sample of 30 radiographs seemed to be sufficient, we included about 200 samples in each group due to the risk of not discovering any resorption and possible statistical problems.

Statistical Analysis

The normality of the distribution was investigated using the Shapiro-Wilk test. Accordingly, the variables were compared according to the normality of the distribution using an independent sample t-test or Mann-Whitney U test. In addition, categorical variables between groups were compared using the chi-square test. Finally, Cohen's Kappa coefficient was calculated for intra- and inter-observer agreement. All statistical analyzes were performed in Jamovi software (version 2.3.18), and a p value of <0.05 was considered statistically significant.

Results

Panoramic radiographs of 424 individuals (236 healthy and 188 epileptic patients) were retrospectively analyzed. Table-1 presents the sociodemographic characteristics of the subjects. The groups demonstrated statistically similar patterns by age and

Table 1 The sociodemographic characteristics

	Overall (N=424)
Groups	
Healthy	236 (55.7%)
Epileptic	188 (44.3%)
Sex	
Male	176 (41.5%)
Female	248 (58.5%)
Age	
< 30 years	228 (53.8%)
> 30 years	196 (46.2%)
Age	
Mean (SD)	29.4 (8.5)
Range	18.0 - 69.0

Table 2 Distribution and comparison of tooth resorption between the groups

	Healthy (N=5793)	Epileptic (N=4297)	Total (N=10090)	p-value
Apical third				
Yes	51.0 (0.9%)	44.0 (1.0%)	95.0 (0.9%)	0.460
No	5742.0 (99.1%)	4253.0 (99.0%)	9995.0 (99.1%)	
Middle third				
Yes	5.0 (0.1%)	13.0 (0.3%)	18.0 (0.2%)	0.011
No	5788.0 (99.9%)	4284.0 (99.7%)	10072.0 (99.8%)	
Cervical third				
Yes	2.0 (0.0%)	1.0 (0.0%)	3.0 (0.0%)	0.746
No	5791.0 (100.0%)	4296.0 (100.0%)	10087.0 (100.0%)	

The presence of resorption is indicated as "yes" and the absence of resorption as "no" in the tables.

gender (p>0.05). Resorption was found in 93 (21.9%) of 424 patients (236 healthy and 188 epileptic patients), but there was no statistical difference between the groups according to age and gender (p=0.018 and p=0.013, respectively). It was determined that epilepsy patients with resorption were using carbamazepine, levesiteram, depakine, lacosamide, lamotrigine, and phenytoin.

Moreover, the groups did not significantly differ in the incidence of external and internal resorption (p = 0.089 and 0.746, respectively) (Table-2). However, we could find a significant difference between the groups by region of resorption (p = 0.011). Accordingly, epileptic patients had more resorption in the middle third region (Table-3).

Table 3 Distribution of the region of tooth resorption location between the groups

	Healthy (N=5793)	Epileptic (N=4297)	Total (N=10090)	p-value
Upper anterior				
Yes	12.0 (0.2%)	10.0 (0.2%)	22.0 (0.2%)	0.785
No	5781.0 (99.8%)	4287.0 (99.8%)	10068.0 (99.8%)	
Upper premolar				
Yes	6.0 (0.1%)	2.0 (0.0%)	8.0 (0.1%)	0.314
No	5787.0 (99.9%)	4295.0 (100.0%)	10082.0 (99.9%)	
Upper molar				
Yes	8.0 (0.1%)	8.0 (0.2%)	16.0 (0.2%)	0.548
No	5785.0 (99.9%)	4289.0 (99.8%)	10074.0 (99.8%)	
Lower anterior				
Yes	6.0 (0.1%)	4.0 (0.1%)	10.0 (0.1%)	0.869
No	5787.0 (99.9%)	4293.0 (99.9%)	10080.0 (99.9%)	
Lower premolar				
Yes	11.0 (0.2%)	4.0 (0.1%)	15.0 (0.1%)	0.212
No	5782.0 (99.8%)	4293.0 (99.9%)	10075.0 (99.9%)	
Lower molar				
Yes	15.0 (0.3%)	27.0 (0.6%)	42.0 (0.4%)	0.004
No	5778.0 (99.7%)	4270.0 (99.4%)	10048.0 (99.6%)	

The presence of resorption is indicated as "yes" and the absence of resorption as "no" in the tables.

Table 4 Distribution of teeth with resorption between the groups

	Healthy (N=5793)	Epileptic (N=4297)	Total (N=10090)	p-value
External				
Yes	56.0 (1.0%)	57.0 (1.3%)	113.0 (1.1%)	0.089
No	5737.0 (99.0%)	4240.0 (98.7%)	9977.0 (98.9%)	
Internal				
Yes	2.0 (0.0%)	1.0 (0.0%)	3.0 (0.0%)	0.746
No	5791.0 (100.0%)	4296.0 (100.0%)	10087.0 (100.0%)	

The presence of resorption is indicated as "yes" and the absence of resorption as "no" in the tables.

In addition, it was concluded that there was a significant difference between the groups according to the resorption distribution. The findings revealed more resorption in the lower molars of the case group (p = 0.004) (Table-4). Considering the incidence of resorption by sex, we found that males had more resorption than females (p = 0.013) (Table-5). Moreover, the prevalence of resorption was significantly more among those aged over 30 years than that among those under 30 years (p =

Table 5 Prevalence of resorption by sex

	Male (N=176)	Female (N=248)	Total (N=424)	p-value
Resorption				
Yes	49.0 (27.8%)	44.0 (17.7%)	93.0 (21.9%)	0.013
No	127.0 (72.2%)	204.0 (82.3%)	331.0 (78.1%)	

The presence of resorption is indicated as "yes" and the absence of resorption as "no" in the tables.

0.018) (Table-6). Finally, the intra-observer and inter-observer kappa values were calculated as 0.90 and 0.92, respectively (almost perfect) (32).

Discussion

Previously, some case reports and few case-control studies explored the link between systemic diseases and drug use and root resorption, frequently external cervical root resorption (28-31, 34, 35). Yet, the literature seems to have missed exploring the prevalence and localization of external and internal root resorption in epileptic patients using AEDs. To the best of our knowledge, this is the first study to evaluate root resorption in patients with epilepsy using antiepileptic drugs.

Our findings did not yield a significant difference in the incidence of external and internal resorption between the groups (p = 0.089). While the incidence of external resorption in epileptic patients was (1.3%), any patients did not have internal resorption (0.0%). Overall, we detected resorption in 93 (21.9%) of 424 participants. A previous case-control study investigated the impacts of the use of a drug called Denosumab on the presence of external cervical resorption and could not conclude a significant difference between the case and control groups (31). In their case-control study, Irinakis et al. traced the prevalence of external root resorption considering imaging methods, oral examination, and local and systemic risk factors and detected the prevalence of external root resorption to be 2.3%. In the same study, the authors reported diabetes as a systemic risk factor and trauma as a local risk factor (35). Dao et al. reported external resorption as the most prevalent (29.3%) and internal resorption as the less prevalent finding (9.6%) in their study on CBCT images of the patients (36). In their study on periapical radiographs of the general population, Tsesis et al. concluded the prevalence of root resorption to be 28.8% (27), while Banica et al. found external root resorption to be the most prevalent (58.4%) among adults with inflammation (37). Moreover, Maninescu et al. showed external root resorption at a rate of 27.07% and internal root resorption at a rate of 0.83% on selected panoramic radiographs (32). On the other hand, Laux et al. detected root resorption at a rate of 19% in radiological evaluation, albeit this rate became 81% as a result of histological evaluations (38). The previous research considered different imaging methods (e.g., periapical radiography, panoramic radiography, and CBCT) and histological methods. Our results seem to overlap with the rates reported in studies exploring panoramic and periapical radiographs. However, CBCT was previously asserted to be more reliable in detecting root resorption (18). Panoramic radiographs have advantages such as low cost and imaging of the entire jaw. It is also used in the diagnosis of root resorption. However, it has disadvantages such as magnification and superposition. These disadvantages may cause errors in the diagnosis of root resorption on panoramic radiographs (32, 36, 39). A disadvantage of panoramic radiography in terms of detecting root resorption may explain the higher prevalence of tooth root resorption observed in CBCT and histological methods compared to panoramic radiographs. The use of panoramic radiographs is a limitation and may have affected our results.

In this study, lower molars were found to be significantly more affected by resorption in the case group (p = 0.004). In addition, we determined the prevalence of tooth root resorption to be significantly higher in the middle third region, males, and those aged over 30 years (p = 0.011, 0.013, and 0.018, respectively). Unlike this study, the research on CBCT images found no significant difference in the prevalence of resorption by age and sex. In the same study, anterior teeth (43.8%) were reported to be the most frequently affected permanent teeth, followed by molar teeth (40.6%) (36). However, Tsesis et al. determined resorption to be the most prevalent in mandibular molars and among patients aged 45 years and older (27). Moreover, another study concluded external

cervical resorption to be more prevalent among men, which was attributed to possible traumatic injuries due to men's engaging in aggressive contact sports and activities more than women (40).

In addition, it was previously demonstrated that the anterior maxillary incisors are affected more frequently, particularly following orthodontic treatment, and that 75.26% of the patients experience apical root resorption. Yet, the same study reported no significant difference between the case and control groups by age and sex (41). In another study, it was reported that asthma patients had an increased prevalence of external apical root resorption following orthodontic treatment (34). In addition, it was determined that experimentally induced osteoporosis in rats caused faster tooth movement and also increased the severity of root resorption compared to the control group (42). In the literature, it is claimed that AEDs reduce the density of jawbone and dental tissues in both animal and human studies (6, 43). However, tooth root resorption has not been evaluated in epileptic patients using AEDs. In this study, unlike healthy subjects, resorption of the lower molars and middle third was more common in epileptic patients, and this may be related to possible adverse effects of AEDs.

Limitations

The use of panoramic radiographs of the cases is the main limitation of this study. We suggest that this study should be performed by knowing drug doses, duration of use and using advanced imaging methods (CBCT), since clinicians are often confronted with epilepsy patients in dental practices. This is a preliminary research. Therefore, future studies with a larger dataset in different drug groups and dental regions are recommended.

Conclusion

Despite no significant difference between epileptic patients and healthy subjects in the prevalence of resorption, we concluded resorption to be the most prevalent in the lower molars and middle third region among the patients.

Conflict of Interest Statement

There is no conflict of interest.

Ethical Approval

Ethical approval of the study was given by the ethics committee of Necmettin Erbakan University, Faculty of Dentistry, Pharmaceutical and Non-Medical Non-device research. (Decision no: 2022-251) This study was conducted in accordance with all versions of the Declaration of Helsinki.

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Availability of Data and Materials

Data is available upon request due to privacy or other restrictions.

Authors Contributions

FPH, KTT, GM: Conceptualization; Data Curation; Formal Analysis; Investigation; Methodology; Validation; Visualization; Writing-Original Draft, Writing-Review and Editing.
GM: Supervision

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