ORIGINAL RESEARCH

Bagcilar Med Bull
DOI: 10.4274/BMB.galenos.2024.2024-03-023

Is Adenoid Hypertrophy Associated with Childhood Afebrile Seizure?

Adenoid Hipertrofisi Çocukluk Çağı Afebril Konvüzyonu ile İlişkili Olabilir mi?

Nur Aycan[1], Harun Arslan[2]

[1]Van Yüzüncü Yıl University Faculty of Medicine, Department of Pediatrics, Van, Turkey
[2]Van Yüzüncü Yıl University Faculty of Medicine, Department of Radiology, Van, Turkey

Abstract

Objective: Afebrile seizures may occur during childhood and may recur with different etiologies. The relationship between hypoxia and disease has been frequently emphasized in the literature. Our aim was to determine whether airway stenosis and adenoid tissue volume are effective in the course of afebrile seizures and, if so, to determine how this relationship is correlated.

Method: Adenoid tissue volume and nasopharyngeal distance were measured from brain magnetic resonance imaging images taken for routine cranial imaging of children aged 2-8 years who presented to the Pediatric Emergency Unit of Van Yüzüncü Yıl University Hospital with afebrile seizures. Demographic characteristics, anticonvulsant drug use, adenoid hypertrophy symptoms, and the number of convulsive episodes were recorded. Statistical analysis was performed on the variables determined.

Results: This study examined 156 children who were admitted to the hospital with afebrile seizures between the specified dates, within the specified age range, and who met the inclusion criteria were examined. The mean ages of the 92 boys and 64 girls were 3.94±0.139 years. No statistically significant intergroup difference was found between the sexes regarding age, number of afebrile seizure episodes, or nasopharyngeal distance (p>0.05). Although 145 (92.9%) of the patients were using only one anticonvulsive drug, 11 (7.1%) were using two anticonvulsive drugs. Adenoid tissue volume dimensions were significantly higher in boys (2.17±0.09) than in girls (1.87±0.12) (p=0.023). There was a statistically significant positive correlation between adenoid volume and the number of afebrile seizure episodes (r=0.586, p=0.0001; n=156).

Conclusion: Increased volumetric adenoid tissue size may be an effective factor in recurrent episodes of childhood afebrile seizure.

Keywords: Adenoid hypertrophia, afebrile seizure, childhood

Öz

Amaç: Afebril konvüzyonlar çocukluk çağında farklı etiyolojilerle ortaya çıkabilmekte, farklı etiyolojilerle tekrar edebilmektedir. Literatürde sıklıkla hipoksi ile hastalığın ilişkisi vurgulanmış olup amacımız hava yolu darlığı ve adenoid doku volümünün afebril konvüzyonların seyrinde etkili olup olmadığını, varsa bu ilişkinin nasıl bir korelasyon gösterdiğini saptamaktır.

Yöntem: Van Yüzüncü Yıl Üniversitesi Hastanesi Çocuk Acil Ünitesi'ne afebril konvüzyon ile başvuran 2-8 yaş arasındaki çocukların rutin kraniyal görüntülemesi için çekilen beyin manyetik rezonans görüntülerinden adenoid doku volümü ve nazofarengeal mesafesi ölçümleri yapıldı. Hastaların demografik özellikleri, antikonvülzan ilaç kullanımları, adenoid hipertrofisi semptomları ve konvülziv atak sayıları kaydedildi. Belirlenen değişkenler açısından istatistiksel analiz yapıldı.

Bulgular: Çalışmada, belirlenen tarihler arasındaki hastanemiz çocuk acil ünitesine afebril konvüzyon ile başvuran, belirlenen yaş aralığındaki ve dahil edilme kriterlerine uygun 156 çocuk retrospektif olarak incelenmiştir. Doksan iki erkek ve 64 kız çocuğunun ortalama yaşı 3,94±0,139 olup cinsiyetler arasında yaş, afebril konvüzyon atak sayısı ve nazofaringeal mesafe açısından istatistiksel anlamlı farklılık saptanmamıştır (p>0,05). Hastaların 145'i (%92,9) sadece bir antikonvülsif ilaç kullanırken, 11'i (%7,1) iki antikonvülsif ilaç kullanmaktaydı. Adenoid doku volüm boyutları erkek çocuklarında (2,17±0,09) kız çocuklarından (1,87±0,12) istatistiksel olarak anlamlı şekilde yüksekti (p=0,023). Çocukların adenoid volümü ve afebril konvüzyon atak sayıları arasında ise istatistiksel olarak anlamlı şekilde pozitif yönde bir korelasyon mevcuttu (r=0,586, p=0,0001; n=156).

Sonuç: Adenoid doku volümetrik boyutlarında artış çocukluk çağı ateşsiz konvüzyon ataklarında etkili faktörlerden biri olarak düşünülebilir.

Anahtar kelimeler: Adenoid hipertrofi, afebril nöbet, çocukluk çağı

Address for Correspondence: Nur Aycan, Van Yüzüncü Yıl University Faculty of Medicine, Department of Pediatrics, Van, Turkey
E-mail: drnaycan@gmail.com **ORCID:** orcid.org/0000-0001-7947-9496 **Received:** 05.03.2024 **Accepted:** 07.07.2024

Cite this article as: Aycan N, Arslan H. Is Adenoid Hypertrophy Associated with Childhood Afebrile Seizure?. Bagcilar Med Bull

Introduction

A seizure is a short-term change in regular electrical activity in the brain that leads to changes in perception, awareness, movement, or behavior (1). Seizures, broadly classified as febrile and non-febrile, account for approximately 1% of emergency department admissions (2). Many underlying pathological causes, such as infections, genetics, traumatic or non-traumatic brain injury, metabolic or electrolyte disturbances, and neurodevelopmental conditions, can result in abnormal neuronal activity even in the absence of fever (3). This aspect adds complexity to clinical assessment and raises questions regarding causes and the probability of recurrence. (4). Afebrile seizures are neurological conditions characterized by the occurrence of two or more seizures with a gap of at least 24 hours between them, often without a known cause. Childhood epilepsy is linked to various additional health issues, such as social-emotional and cognitive difficulties (5). Longer seizure duration, hyperglycemia, age at onset ≥11 years, and acidosis were predictive of seizure recurrence in children with new-onset afebrile seizures (6). Abnormal electroencephalography (EEG) findings are also considered in the risk of recurrence (7)

Adenoid hypertrophy is usually self-limiting and resolves during puberty when adenoids atrophy and regress (8). Diagnosis of adenoid tissue size with infectious and non-infectious etiologies can be performed with lateral direct radiography or flexible nasopharyngoscopy without the risk of radiation using a reliable and satisfactory method (9,10). It may cause narrowing of the passage in the upper respiratory tract and may lead to undesirable long-term effects if not treated at the appropriate time (11). In the literature, cognitive impairment in patients with adenoid hypertrophy has also been shown to be reversed by adenoidectomy (12), and amygdala/hippocampus volume ratios were higher in children with adenotonsillar hypertrophia-induced obstructive sleep apnea syndrome (OSAS) (13). Because intermittent hypoxemia may cause changes in some brain structures, we aimed to determine whether there is a relationship between unprovoked afebrile seizures and adenoid tissue volume.

Materials and Methods

Subjects

Between 1/9/2018 and 1/5/2021, patients between 2 and 8 years of age admitted to the pediatric emergency unit with afebrile seizure, with no cerebral pathology on routine brain magnetic resonance imaging (MRI) imaging and no biochemical pathology on laboratory tests were included after ethics committee approval (2023/11-12). Patients under 2 years and over 8 years of age, patients with febrile seizure, patients with congenital cerebral anomalies, and patients with intracranial mass, bleeding, demyelinating, and metabolic diseases were not included.

Volumetric Adenoid Measurements

By a radiologist with 10 years of experience, raw images were converted to multiplayer reformation images in an magnetic resonance (Siemens magnetom, Altea, 1.5T, Germany) workplace. The area of the adenoid tissue entering each cross-sectional area from right to left on the sagittal images was measured by manual method, and the areas were combined with the volume generation module in preset settings, and the data obtained were recorded in cubic centimeters.

Statisticsal Analysis

Descriptive statistics were used to summarize continuous variables, including mean, standard error, median, and interquartile range. Categorical variables were summarized using counts and percentages. The Mann-Whitney U test was employed to compare non-categorical variables with continuous variables. Pearson correlation coefficients were computed to assess the relationships between continuous variables. Statistical significance was set at 5%, and calculations were conducted using the SPSS (IBM; version 26) statistical software package.

This study did not receive financial support, and there are no conflicts of interest among the authors. The Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee approved the study (no: 2023/11-12).

Results

A total of 156 children in the specified age range who presented to the Pediatric Emergency Unit of Van Yüzüncü Yıl Hospital with afebrile seizure between the specified dates and who met the inclusion criteria were determined.

The mean age of 92 (58.9%) boys and 64 (41.1%) girls was 3.94±0.139 years, and no statistically significant difference was found between the sexes in terms of age, number of afebrile seizure episodes, and nasopharyngeal distance ($p>0.05$). Although 145 (92.9%) of the patients were using only one anticonvulsive drug, 11 (7.1%) were using two anticonvulsive drugs. All patients were taking their medication regularly. Eighty-five (54.4%) patients

were being treated with sodium valproate, 28 (17.9%) with phenobarbital, and 36 (23%) with levetiracetam. Seven (4.5%) patients were receiving dual combinations of different antiepileptic drugs. All patients were taking their medications regularly.

Adenoid tissue volume dimensions were significantly higher in boys (2.17±0.09: mean ± stderror) than in girls (1.87±0.12; mean ± stderror) (p=0.023) (Table 1). There was a statistically significant positive correlation between adenoid volume and the number of afebrile seizure episodes (r=0.586, p=0.0001; n=156) (Figure 1).

Discussion

Conditions affecting the central nervous system, which both develop intensively from childhood to adolescence and are most vulnerable to injury in childhood, can lead to problems such as attention deficit, autism spectrum disorder, developmental delay, learning difficulties, cerebral palsy, and seizures (14-16). Seizures were ranked among the prevalent neurological conditions observed in pediatric emergency units. Timely identification of epilepsy onset in children experiencing non-fever-related seizures is of paramount importance (17). When assessing the first occurrence of afebrile seizures in children, according to the recommendations of the American Academy of Neurology, it is advised to include EEG and neuroimaging examinations as part of neurodiagnostic assessments (18,19).

Table 1. Age, adenoid volume, and seizure episodes according to gender

	Gender	n	Median (IQR)	Mean rank	p
Age	Male	92	4 (2.75)	80.57	0.483
	Female	64	3 (3)	75.52	
Adenoid volume	Male	92	2 (1.38)	85.37	0.023
	Female	64	1.7 (1.27)	68.63	
Nasopharyngeal distance	Male	92	2.1 (1.68)	74.64	0.201
	Female	64	2.3 (2.5)	84.05	
Seizure recurrence	Male	92	3 (1)	83.63	0.068
	Female	64	3 (1)	71.13	

IQR: Interquartile range

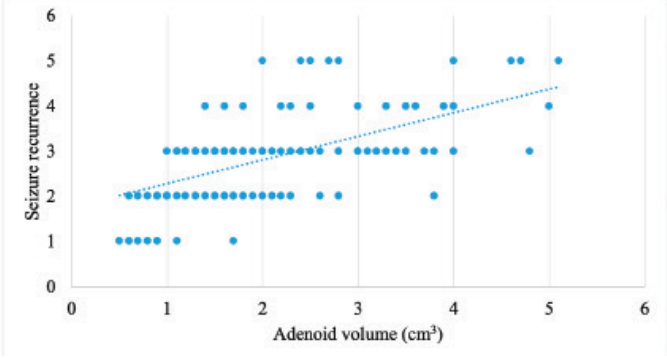

Figure 1. Seizure recurrence and adenoid volume

In a study in which the determinants of abnormal electroencephalogram and neuroimaging findings were investigated in children admitted to the emergency department with afebrile seizures, the number of boys and girls was almost equal (4), whereas in our patient group, male patients were more common. In a study published in 2015 from a center in Japan, when the recurrence risks of patients aged between 1 month and 15 years who were followed up for at least 2 years after the first unprovoked seizure were evaluated, partial seizures were found to be statistically significant compared with generalized seizures in terms of recurrence. Children with focal discharges had significantly more recurrences than those with normal EEGs (20). The risks of recurrence of afebrile seizures include lethargy and lactate elevation, duration of the seizure, and age at onset (17). Age at onset ≥11 years, acidosis, longer seizure duration, and hyperglycemia were predictors of seizure recurrence in children who experienced their first afebrile seizure (6). The relationship between seizure susceptibility and chronic hypoxia has also been shown in recent years. Long-term oxygen deprivation does not just initiate the activation and proliferation of microglia and astrocytes due to oxidative stress and neuroinflammation; it also leads to neuronal excitotoxicity by suppressing sodium and potassium ATP activity, elevating blood-brain barrier permeability, altering ion transporter expression, and diminishing cerebral blood flow (16).

Adenoids, lymphoid tissue known as part of the Waldeyer ring, can cause OSAS, chronic sinusitis, otitis, developmental anomalies in the craniofacial region, speech disorders, and articulation errors. It is also known that oxygen saturation is affected, and hypoxic status occurs due to airway obstruction and respiratory difficulties in people with enlarged adenoid tissue associated with different causes (11,13,15). Finger palpation and oral examination of adenoids using a mirror or direct radiography of the lateral nasopharynx are frequently used to detect adenoid tissue (21,22). In recent years, nasal endoscopy has also been widely used for diagnosis (23). Although MRI is not a routine procedure for nasopharyngeal adenoid hypertrophy, it is often used in head and neck imaging studies. When the cranio-caudal, left-right, and anterior-posterior dimensions of nasopharyngeal adenoid tissues in

approximately 6700 MRIs taken in the same health center between 0-82 ages are measured, it has been shown that adenoid tissue significantly regresses with age in head/neck MRI imaging performed for different reasons in different age groups. The cranio-caudal and left-right sizes of nasopharyngeal adenoid hypertrophy were largest in 0-9 years and decreased with age (24). On the other hand, in a different study, it was declared to disappear completely in adulthood. This study evaluated 189 patients who were referred for brain MRI scan with no history or clinical evidence of adenoid disease to determine the age-specific appearance of normal adenoid tissue, as measured on sagittal T1-weighted midline MRI images (25). In animal model studies, obstructive sleep apnea was found to induce neuronal cell loss in several brain regions, resulting in brain regions leading to changes in mood and cognition functions, particularly in the pediatric age. A review of the available evidence shows that many of the arguments in favor of causality converge and support the notion that OSA can cause both reversible and irreversible neural damage and functional impairments (26). In a study including 10 children with polysomnographically confirmed OSA and 8 healthy controls of similar age and sex with no evidence of sleep-disordered breathing in an overnight sleep study, Kheirandish-Gozal et al. (27) reported that several brain regions in children with obstructive sleep apnea, including the middle and posterior corpus callosum, prefrontal cortex, hippocampus, thalamus, and cerebellar areas, demonstrated decreased entropy values. MRI alterations pointed to acute pathological impacts caused by obstructive sleep apnea (27). In a comparative study of 100 patients with adenotonsillar hypertrophy and OSAS and 100 healthy children in the same age group, children with adenotonsillar hypertrophy and OSAS displayed greater amygdala sizes and ratios of amygdala to hippocampus volumes compared with their healthy counterparts. However, their hippocampal volumes were comparatively lower. Additionally, there was a correlation between the duration of the disease and the presence of hypoxemia conditions with amygdala/hippocampus volume ratios. Apnea-hypopnea index and SaO2 <90% were significantly positively correlated with amygdala and hippocampus ratios (13). Canessa et al. (28) examined the brain structures of children with OSA and discovered reduced volumes in several brain regions, including the hippocampus, left posterior parietal cortex, and right superior frontal gyrus, compared with the healthy control group. This study of 17 children with OSA demonstrated for the first time the existence of structural brain abnormalities in regions vulnerable to hypoxemia that can be altered by treatment (28). We believe that adenoid tissue, which causes oxygen changes with the narrowing of the airway passage, is associated with childhood afebrile seizures. With these data in the future, there will be advances in research that will make progress on whether individualized therapies exist to deepen the relationship between chronic hypoxia, which we know increases neuronal excitability, and seizure susceptibility.

Study Limitations

The validity of our retrospective study is an important limitation. In the future, follow-up according to seizure type, EEG findings, and sleep disorders in a wider age range and prospective follow-up will help obtain more detailed results.

Conclusion

Since no study on adenoid dimensions, afebrile convulsions, and seizure attacks has been found in the literature to the best of our knowledge, our study showed that adenoid volumetric may be among the factors that cause recurrence in children with seizures, and adenoid size should be kept in mind as a risk factor for seizure recurrence.

Ethics

Ethics Committee Approval: This study did not receive financial support, and there are no conflicts of interest among the authors. The Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee approved the study (no: 2023/11-12).

Informed Consent: The consent of the patients has been obtained.

Authorship Contributions

Surgical and Medical Practices: N.A., Concept: H.A., Design: N.A., H.A., Data Collection or Processing: H.A., Analysis or Interpretation: N.A., H.A., Literature Search: H.A., Writing: N.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Abdennadher M, Saxena A, Pavlova MK. Evaluation and Management of First-Time Seizure in Adults. Semin Neurol. 2021;41(5):477-482.

2. Chen CY, Chang YJ, Wu HP. New-onset seizures in pediatric emergency. Pediatr Neonatol. 2010;51(2):103-111.

3. Hsieh DT, Chang T, Tsuchida TN, Vezina LG, Vanderver A, Siedel J, et al. New-onset afebrile seizures in infants: role of neuroimaging. Neurology. 2010;74(2):150-156.

4. Ali N, Haider S, Mustahsan S, Shaikh M, Raheem A, Soomar SM, et al. Predictors of abnormal electroencephalogram and neuroimaging in children presenting to the emergency department with new-onset afebrile seizures. BMC Pediatr. 2022;22(1):619.

5. Bailey K, Im-Bolter N. Social context as a risk factor for psychopathology in children with epilepsy. Seizure. 2018;57:14-21.

6. Woo S, Nah S, Kim M, Moon J, Han S. Predictors of seizure recurrence in emergency department pediatric patients with first-onset afebrile seizure: A retrospective observational study. Am J Emerg Med. 2021;50:316-321.

7. Kanemura H, Mizorogi S, Aoyagi K, Sugita K, Aihara M. EEG characteristics predict subsequent epilepsy in children with febrile seizure. Brain Dev. 2012;34:302-307.

8. Goeringer GC, Vidić B. The embryogenesis and anatomy of Waldeyer's ring. Otolaryngol Clin North Am. 1987;20(2):207-217.

9. Talebian S, Sharifzadeh G, Vakili I, Golboie SH. Comparison of adenoid size in lateral radiographic, pathologic, and endoscopic measurements. Electron Physician. 2018;10(6):6935-6941.

10. Geiger Z, Gupta N. Adenoid Hypertrophy. [Updated 2023 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536984/

11. Niedzielski A, Chmielik LP, Mielnik-Niedzielska G, Kasprzyk A, Bogusławska J. Adenoid hypertrophy in children: a narrative review of pathogenesis and clinical relevance. BMJ Paediatr Open. 2023;7(1):e001710.

12. N Thabit M, Elnady HM, S Badawy B, Mahmoud HA. Cognitive Event-Related Potentials in Patients With Adenoid Hypertrophy: A Case-Control Pilot Study. J Clin Neurophysiol. 2016;33(5):443-449.

13. Ma Y, Niu Z, Ruan L, Xue S, Li N, Yao X, et al. Alterations in Amygdala/Hippocampal Volume Ratios in Children with Obstructive Sleep Apnea Syndrome Caused by Adenotonsillar Hypertrophy. Med Sci Monit. 2023;29:e937420.

14. Terraneo L, Samaja M. Comparative Response of Brain to Chronic Hypoxia and Hyperoxia. Int J Mol Sci. 2017;18(9):1914.

15. Wu J, Gu M, Chen S, Chen W, Ni K, Xu H, et al. Factors related to pediatric obstructive sleep apnea-hypopnea syndrome in children with attention deficit hyperactivity disorder in different age groups. Medicine (Baltimore). 2017;96:e8281

16. Xu Y, Fan Q. Relationship between chronic hypoxia and seizure susceptibility. CNS Neurosci Ther. 2022;28(11):1689-1705.

17. Woo S, Nah S, Kim M, Kim S, Lee D, Moon J, et al. Risk of Epilepsy in Children Presenting to Emergency Departments with Their First Afebrile Seizure: A Retrospective Multicenter Study. Children (Basel). 2022;9(11):1741.

18. Hirtz D, Ashwal S, Berg A, Bettis D, Camfield C, Camfield P, et al. Practice parameter: evaluating a first nonfebrile seizure in children: report of the quality standards subcommittee of the American Academy of Neurology, The Child Neurology Society, and The American Epilepsy Society. Neurology. 2000;55(5):616-623.

19. Kim GU, Park WT, Chang MC, Lee GW. Diagnostic Technology for Spine Pathology. Asian Spine J. 2022;16(5):764-775.

20. Mizorogi S, Kanemura H, Sano F, Sugita K, Aihara M. Risk factors for seizure recurrence in children after first unprovoked seizure. Pediatr Int. 2015;57(4):665-669.

21. Brandtzaeg P. Immunology of tonsils and adenoids: everything the ENT surgeon needs to know. Int J Pediatr Otorhinolaryngol. 2003;67:69-76.

22. van den Akker EH, Sanders EA, van Staaij BK, Rijkers GT, Rovers MM, Hoes AW, et al. Long-term effects of pediatric adenotonsiilectomy on serum immunoglobulin levels: results of randomized controlled trial. Ann Allergy Asthma Immunol. 2006;97(2):251-256.

23. Berlucchi M, Salsi D, Valetti L, Parrinello G, Nicolai P. The role of mometasone furoate aqueous nasal spray in the treatment of adenoidal hypertrophy in the pediatric age group: preliminary results of a prospective, randomized study. Pediatrics. 2007;119(6):1392-1397.

24. Surov A, Ryl I, Bartel-Friedrich S, Wienke A, Kösling S. MRI of nasopharyngeal adenoid hypertrophy. Neuroradiol J. 2016;29(5):408-412.

25. Vogler RC, Ii FJ, Pilgram TK. Age-specific size of the normal adenoid pad on magnetic resonance imaging. Clin Otolaryngol Allied Sci. 2000;25(5):392-395.

26. Gozal D. CrossTalk proposal: the intermittent hypoxia attending severe obstructive sleep apnoea does lead to alterations in brain structure and function. J Physiol. 2013;591:379-381.

27. Kheirandish-Gozal L, Sahib AK, Macey PM, Philby MF, Gozal D, Kumar R. Regional brain tissue integrity in pediatric obstructive sleep apnea. Neurosci Lett. 2018;682:118-123.

28. Canessa N, Castronovo V, Cappa SF, Aloia MS, Marelli S, Falini A, et al. Obstructive sleep apnea: Brain structural changes and neurocognitive function before and after treatment. Am J Respir Crit Care Med. 2011;183:1419-1426.