Original Article

J Korean Child Neurol Soc 2017;25(3):127-132
https://doi.org/10.26815/jkcns.2017.25.3.127
pISSN 1226-6884•eISSN 2383-8973

국소 겉질 형성이상으로 인한 소아 뇌전증 환자에서 뇌전증 수술 후 항경련제 복용 중단

연세대학교 의과대학 소아과학교실 세브란스 어린이병원 소아신경과[1], 연세대학교 의과대학 신경외과학교실 소아신경외과[2]
서세은[1] · 김세희[1] · 김동석[2] · 강훈철[1] · 이준수[1] · 김흥동[1]

Discontinuing Antiepileptic Drugs after Pediatric Epilepsy Surgery for Focal Cortical Dysplasia

Purpose: Antiepileptic drugs (AEDs) can be discontinued in a subset of patients after surgery. We aimed to identify the factors related to successful AED withdrawal after surgery in pediatric patients with focal cortical dysplasia (FCD).
Methods: The study included 134 patients who underwent resective surgery for FCD at Severance Hospital between 2003 and 2014. Age of seizure onset, epilepsy duration, and location and histopathological classification of the FCD were compared between patients who experienced seizure recurrence and those who did not. The interval between surgery and initiation of AED reduction was also compared.
Results: In total, 134 patients were included. The median age at seizure onset was 1.0 year (interquartile range [IQR], 0.3–5.0). The median follow-up duration was 6.0 years (IQR, 1.0–13.0). AED withdrawal was attempted in 89 (66%), and 61 (69%) patients remained seizure-free. Of 61 patients, 38 (62%) were successfully weaned off all AEDs. Seizures recurred in 28 (31%) patients. The mean duration between surgery and initiation of AED reduction did not significantly differ between the seizure recurrence (4.5 months, IQR, 2.7–8.7) and non-recurrence groups (1.9 months, IQR, 0.5–5.4) (P<0.006). Patients who had FCD type IIb (39% vs. 7%, P=0.004) were more likely to be in the non-recurrence group than in the recurrence group (P=0.031).
Conclusion: Surgical resection offers patients with FCD an opportunity to completely discontinue their AEDs. Early AED discontinuation may be pursued in patients with FCD in cases of complete resection.

Key Words: Focal cortical dysplasia, Epilepsy surgery, Pediatric, Antiepileptic drugs, Withdraw, Reduce

Se Eun Seo, MD[1], Se Hee Kim, MD[1], Dong Suk Kim, MD, PhD[2], Hoon-Chul Kang, MD, PhD[1], Joon Soo Lee, MD, PhD[1], Heung Dong Kim, MD, PhD[1]

[1]Division of Pediatric Neurology, Department of Pediatrics, Pediatric Epilepsy Clinic, Severance Children's Hospital, Yonsei University College of Medicine, Seoul, Korea, [2]Division of Pediatric Neurosurgery, Department of Neurosurgery, Severance Children's Hospital, Yonsei University College of Medicine, Seoul, Korea

Submitted: 31 May, 2017
Revised: 27 July, 2017
Accepted: 27 July, 2017

Correspondence to Se Hee Kim, MD
Division of Pediatric Neurology, Department of Pediatrics, Severance Hospital, Yonsei University College of Medicine, 50-1, Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: +82-2-2228-2050, Fax: 82-2-393-9118
E-mail: SEHEEKIM@yuhs.ac

Introduction

Epilepsy surgery remains the most effective treatment option for medically intractable epilepsy in children and adults[1)]. The most common etiologies of the types of epilepsy observed in pediatric surgical candidates are focal cortical dysplasia (FCD), low-grade tumors, and hippocampal sclerosis[2)].

FCDs comprise a spectrum of focal developmental malformations characterized by disruption of the normal cytoarchitecture of the cerebral

cortex. They are highly associated with medically intractable epilepsy and recognized to be the most common indication for pediatric epilepsy surgery[3].

Currently, there are no clear guidelines for the withdrawal of antiepileptic drugs (AEDs) after epilepsy surgery in patients with FCD, resulting in variations in the implementation of this withdrawal among physicians. Many physicians continue to administer AEDs despite successful surgery, owing to concerns regarding seizure recurrence upon AED withdrawal, as well as the possibility of failure to control seizures despite the readministration of AEDs[4].

A previous study showed that the tapering and discontinuation of AEDs may be considered in patients with epilepsy who have been seizure-free for 2 to 5 years[5]. However, recent studies suggest that earlier AED withdrawal may be possible if the primary epileptic focus is completely resected[6]. Other recent reports have shown that the majority of US and Canadian epileptologists and neurologists prefer to wait for 6 months to 2 years before introducing any changes in medication[7]. Previous studies regarding AED discontinuation after epilepsy surgery examined the number of patients in whom the tapering and discontinuation of AEDs was successful as well as the rate of seizure relapse among these patients[6,8-13]. However, to the best of our knowledge, no study has analyzed this phenomenon exclusively in pediatric patients with FCD despite its differences in pathology, and disease course and prognosis from other epilepsy-related lesions.

The purpose of the present study was to identify the rate of successful AED withdrawal after FCD resective surgery, as well as the predictors of seizure recurrence in pediatric patients with intractable epilepsy due to FCD. We also aimed to evaluate the appropriate timing for AED withdrawal and to determine which patients may be eligible for early AED withdrawal.

Materials and Methods

1. Patients

Patients who underwent epilepsy surgery at Severance Children's Hospital between May 1, 2003 and September 1, 2014 were included in the present study. Patients were included if they met the following criteria: (1) pathologically confirmed FCD type I or II; (2) drug-resistant epilepsy, defined as uncontrolled seizures despite use of two appropriate AEDs; (3) seizure onset at the age of 18 years or younger; and (4) a minimum of 1 year of follow-up. Patients who underwent lesionectomy, lobectomy, and multilobar resections were included. Patients were excluded if they showed lesions consistent with FCD only on magnetic resonance imaging (MRI). Patients were also excluded if they had pathologically confirmed FCD type III, because the combined epileptogenic lesions were heterogeneous. Finally, patients who received corpus callosotomy or implantation of a vagal nerve stimulator were excluded. Diagnosis and classification of FCDs were made based on the 2011 International League Against Epilepsy classification[3]. The study was approved by the Institutional Review Board of Yonsei University Health Service, Severance Hospital (IRB approval number: No. 4-2017-0253).

2. Procedures

To identify factors predictive of successful AED withdrawal, the following data were reviewed: age at seizure onset, sex, interval between seizure onset and surgery, location of the surgery, histopathological classification of the resected tissue, postoperative electroencephalogram (EEG) abnormalities, and interval from surgery to the initiation of AED reduction. These factors were compared between patients who achieved freedom from seizures after surgery and those who did not. In order to identify factors that affect a physician's decision to begin AED reduction, patients who underwent AED reduction were compared with those who did not. Subsequently, factors were compared between patients who completed AED withdrawal and patients who experienced seizure recurrence in relation to AED reduction.

Seizure outcome data based on the Engel criteria were collected at each visit[14]. Routine postsurgical follow-up included outpatient visits at 3 months, 6 months, and 1 year. After 1 year, regular follow-up was performed every 6 to 12 months for patients who achieved seizure freedom. Seizure freedom was defined as absence of clinical seizures and auras after surgery until the last follow-up. Seizure recurrence was defined as reappearance of a clinical seizure after the initiation of AED in patients who achieved seizure freedom after surgery.

Postoperative EEG abnormalities were assessed using 30-minute (routine) EEG recordings and ambulatory 4-hour EEG recordings. From the EEG recordings, background activity and epileptiform discharges including sharp waves, spikes, and paroxysmal fast activities were reviewed. The 10-20 system of electrode placement was used. The EEG data were analyzed using TWin EEG software (Natus/Grass Technologies Ltd., Warwick, RI, USA).

3. Statistical analysis

For comparisons between each group, chi-squared analysis, Fisher's exact test, and Student's t-test were used to analyze numerical variables. For the univariate analysis of FCD types, a standard forward stepwise Kaplan-Meier analysis was performed.

Data were obtained from electronic medical records. *P* values <0.05 were regarded as statistically significant. The data storage and statistical analyses were performed with SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). Values were expressed as number (%), mean±standard deviation (SD), or median (interquartile range [IQR]).

Results

In total, 134 patients with FCD underwent epilepsy surgery. Median age at seizure onset was 1.0 (IQR, 0.3–5.0) years. The patients included 80 boys and 54 girls. The median age of patients who underwent surgery was 7.0 (IQR, 3.0–12.0) years. Of the 134 patients, 52 had FCD type I, 57 had FCD type IIa, and 25 had FCD type IIb. The median follow-up duration was 6.0 years (IQR, 1.0–13.0). The median number of AEDs used before surgery was 3.0 (IQR, 1.0–5.0) (Table 1).

Among the 134 patients, 106 (79%) patients initially achieved seizure freedom, and AED reduction was attempted in 89 (66%) after a median duration of 3.5 months following epilepsy surgery. Of these 89 patients, 61 (69%) maintained a seizure-free state. In the seizure-free group, 38 (62%) patients were successfully tapered off all AEDs, and 23 (38%) patients maintained seizure freedom with lower doses of AEDs. Seizure recurrence was observed in 28 (31%) of the 89 patients in whom AED reduction was attempted. In the seizure recurrence group, seizure control or seizure reduction was regained with readjustment of AEDs in 24 patients, while 4 patients experienced persistence or exacerbation of seizures (Fig. 1).

Reduction of AEDs was more likely to be attempted postoperatively in patients with FCD type IIb (24% vs. 9%, *P*=0.039). Other factors including age at seizure onset, age at surgery, and location of the lesions were not related to attempts to reduce AEDs (Table 2).

To identify factors that predicted seizure recurrence, patients who were successfully weaned off all AEDs were compared with those who experienced seizure recurrence after AED reduction

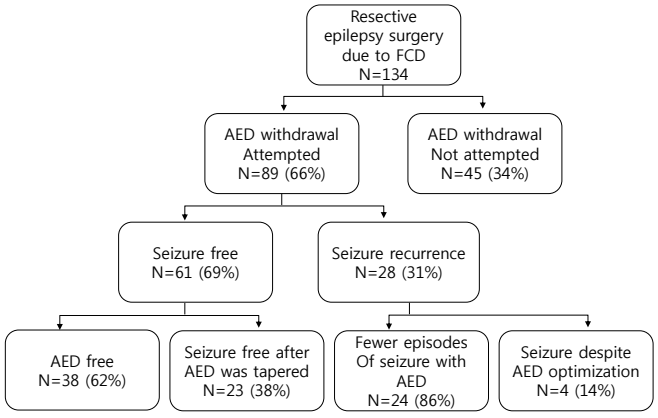

Fig 1. Study population.

Table 1. Baseline Characteristics

Total N of patients	134
Female	54
Age at epilepsy onset (years)	1.0 (0.3–5.0)
Interval between seizure onset and surgery (years)	4.0 (1.7–7.6)
Age at surgery (years)	7.0 (3.0–12.0)
Side of the resected area (Left:Right)	80:54
N of AEDs used before surgery	3.0 (1.0–5.0)
N of AEDs used after surgery	1.0 (0–6.0)
Interval between surgery and start of AED reduction (months)	3.8 (1.3–13.5)
Interval between start of AED reduction and last follow-up (years)	3.6 (1.0–12.4)
Lobar surgery location, N (%)	
Temporal	8 (6)
Frontal	49 (37)
Parietal	8 (6)
Occipital	6 (4)
Bilobar or multilobar	63 (47)
FCD type, N (%)	
FCD type I	52 (39)
FCD type IIa	57 (43)
FCD type IIb	25 (19)

N, number; AEDs, antiepileptic drugs; FCD, focal cortical dysplasia.
Values are described as number (%) or median (interquartile range).

Table 2. Clinical Factors Influencing Start of Antiepileptic Drugs Withdrawal

	Started AED withdrawal (n=89)	Did not start AED withdrawal (n=45)	*P* Value
Female	37	17	0.672
Age at epilepsy onset (years)	0.8 (0.3–5.0)	1.0 (0.2–4.5)	0.865
Interval between seizure onset and surgery (years)	3.2 (1.3–7.7)	5.0 (2.7–8.0)	0.158
Age at surgery (years)	7.0 (2.5–12.0)	7.0 (3.5–12.0)	0.599
Side of the resected area (Left:Right)	57:32	23:22	0.149
N of AEDs used before surgery	3.0 (2.0–4.0)	3.0 (2.0–4.0)	0.749
N of AEDs used after surgery	1.0 (0–2.0)	3.0 (2.0–4.0)	0.743
Surgery location, N (%)			
Temporal	6 (7)	2 (4)	0.596
Frontal	37 (41)	12 (27)	0.091
Parietal	5 (6)	3 (7)	0.809
Occipital	4 (5)	2 (4)	0.989
Bilobar or multilobar	37 (42)	26 (58)	0.076
FCD type, N (%)			
FCD type I	35 (39)	17 (38)	0.833
FCD type IIa	33 (37)	24 (53)	0.072
FCD type IIb	21 (24)	4 (9)	0.039

AED, antiepileptic drugs; N, number; FCD, focal cortical dysplasia.
Values are described as number (%) or median (interquartile range).

(Table 3). Younger age at epilepsy onset (1.0 [0.3–5.0] vs. 1.1 [0.3–3.8] years, $P<0.001$), shorter duration of epilepsy (1.9 [0.5–5.4] vs. 4.5 [2.7–8.7] years, $P=0.006$), and lower number of preoperative AEDs (3.0 [2.0–3.3] vs. 4.0 [3.0–4.0], $P<0.001$) were found in patients who were successfully weaned off all AEDs compared to patients who experienced seizure recurrence. Patients were more likely to experience seizure recurrence if they underwent multilobar resection (54% vs. 29%, $P=0.043$) or had FCD type I (24% vs. 57%, $P=0.010$), while patients were more likely to remain in a seizure-free state after AED reduction if they had FCD type IIb (39% vs.7%, $P=0.004$). Interestingly, the interval between epilepsy surgery and the AED reduction trial was shorter in patients who maintained a seizure-free state than in patients who experienced seizure recurrence (1.6 [0.9–12.5] vs. 4.1 [2.8–6.0] years, $P<0.001$).

AED reduction was started <3 months postoperatively for 39 of 89 patients. Seizure recurrence occurred in 26% of these patients. Moreover, the AED was tapered between 3 and 6 months in 23 patients, between 6 and 12 months in 7 patients, between 12 and 24 months in 13 patients, and after 24 months in 7 patients. The group that underwent early AED tapering (<3 months postoperatively) had a low seizure recurrence rate (26%, $P=0.296$) while patients who underwent later AED tapering (≥24 months postoperatively) had a high seizure recurrence rate (57%, $P=0.127$). Early AED tapering was not associated with a higher incidence of seizure recurrence.

Table 3. Factors Related to Complete Antiepileptic Drugs Withdrawal after Surgery

	Complete AED withdrawal (n=38)	Seizure recurrence before or after AED withdrawal (n=28)	*P* Value
Female	17	11	0.802
Age at epilepsy onset (years)	1.0 (0.3–5.0)	1.1 (0.3–3.8)	<0.001
Interval between seizure onset and surgery (years)	1.9 (0.5–5.4)	4.5 (2.7–8.7)	0.006
Age at surgery (years)	6.5 (2.0–9.8)	8.5 (3.5–12.0)	0.200
Side of the resected area (Left:Right)	26:12	22:6	0.413
N of AEDs used before surgery	3.0 (2.0-3.3)	4.0 (3.0–4.0)	<0.001
Surgery location, N (%)			
Temporal	3 (8)	1 (4)	0.631
Frontal	19 (50)	9 (32)	0.208
Parietal	3 (8)	2 (7)	1.000
Occipital	2 (5)	1 (4)	1.000
Bilobar or multilobar	11 (29)	15 (54)	0.043
FCD type, N (%)			
FCD type I	9 (24)	16 (57)	0.010
FCD type IIa	14 (37)	10 (36)	0.925
FCD type IIb	15 (39)	2 (7)	0.004
Interval between surgery and start of AED reduction (months)	1.6 (0.9–12.5)	4.1 (2.8–6.0)	<0.001

AED, antiepileptic drugs; N, number; FCD, focal cortical dysplasia.
Values are described as number (%) or median (interquartile range).

Background activity and epileptiform discharges on postoperative follow-up EEGs were also reviewed. Patients who did not show interictal epileptiform discharges (IEDs) were more likely to remain in a seizure-free state following tapering off of AEDs (19/26, 73%) than the patients who showed IEDs (42/63, 67%, $P=0.031$). We did not find a significant relationship between presence of IEDs and timing of AED withdrawal (2.8 vs. 3.1 months, $P<0.001$).

The rate of seizure-free survival over time following surgery was analyzed according to FCD subtype using Kaplan-Meier survival curves. Patients with FCD type IIb were more likely to remain seizure-free after AED reduction (31%, $P=0.013$) (Fig. 2), and patients who underwent multilobar resection were more likely to experience seizure recurrence after AED reduction (54 %, $P=0.043$) (Table 3). Age, number of AEDs taken before surgery, frequency of seizures before attempting AED tapering, and brain MRI findings did not affect seizure recurrence after AED withdrawal.

Discussion

After surgery, patients with FCD were more likely to complete AED discontinuation if FCD type was IIb, duration of epilepsy was short, and number of preoperatively used AEDs was small. Delayed start of AED reduction was not associated with successful AED discontinuation.

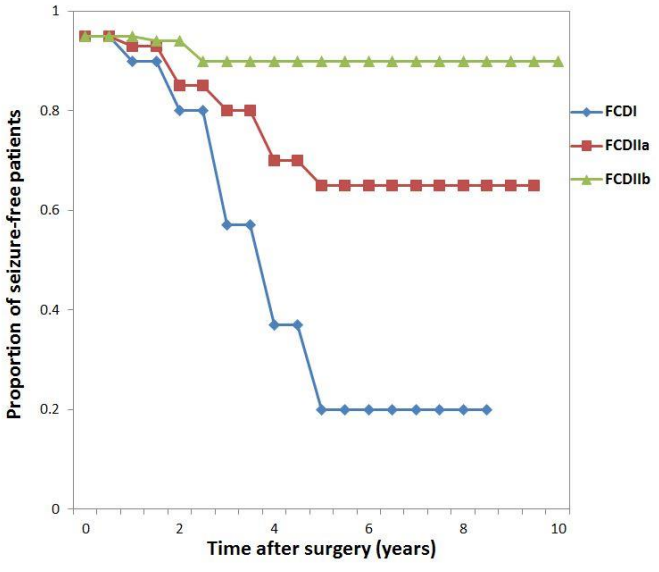

Fig. 2. Kaplan-meier survival vurves for the rate of seizure free patients for each focal cortical dysplasia subtype.

Previous studies analyzed discontinuation of AEDs after surgery in a heterogeneous group of patients with epilepsy. The relapse rates observed in these previous studies were similar to those seen in the present study, ranging between 12 and 44%[12-13,15-17]. Successful AED reduction could be achieved in patients regardless of the timing of this reduction[18]. Our study suggests that AED withdrawal following surgery in patients with FCD can be performed in a similar manner to that in patients with other epileptogenic regions. To the best of our knowledge, this study is the first to analyze AED withdrawal rates only in cases of FCD.

AED reduction was more likely to be attempted in patients who had frontal lobe FCDs, and type IIb FCDs. Complete AED discontinuation could be achieved more frequently in patients with type IIb FCDs. A previous study suggested more successful AED discontinuation in patients with temporal lesions than in those with extratemporal lesions, but we did not observe this trend in our study[19]. Another study also failed to find a similar relationship between FCD location and successful AED discontinuation[6].

In the present study, slow withdrawal of AEDs was not associated with successful AED reduction and seizure freedom. The mean duration between surgery and initiation of AED reduction did not significantly differ between the seizure recurrence and seizure-free groups. In contrast to the findings of this study, however, the results of a previous study showed that delayed timing of AED reduction increased successful AED withdrawal and seizure outcomes[6]. However, our results were concordant with the findings of a recent study that analyzed patients with epilepsy in general[18].

Postoperative EEGs were obtained to screen for background activity and the presence of epileptiform discharges in all patients in the present study. The absence of epileptiform discharges on the EEG was significantly associated with successful AED reduction (P=0.031). Thus, the electrophysiologic variables tested proved to be a significant predictor of seizure recurrence in our patients. However, previous reports have claimed that there are no significant differences in the rate of seizure recurrence between patients with and without epileptic spikes on the postoperative EEG[9,11].

In previous studies, factors associated with successful AED withdrawal were age at seizure onset, duration of epilepsy, brain MRI findings, postoperative EEG results, timing of AED tapering, and location of pathology[7,9,20,21]. However, the factors that showed a significant effect differed among studies. In some studies, successful discontinuation was more common among younger patients and those with a shorter duration of epilepsy[22]. A previous study reported that a longer duration of epilepsy prior to surgery, abnormal postoperative EEG findings, and early postoperative seizures predispose to seizure recurrence[10]. However, these findings were not statistically significant in the present study.

We acknowledge the following limitations of our study. Selection bias may have influenced the study population for AED withdrawal because our epilepsy center is a referral center for patients with severe drug-resistant epilepsy. The data may not be representative for other more benign conditions. In addition, all cases of seizures after surgery were considered a recurrence. This may have resulted in an underestimation of seizure freedom, as fever-triggered or acute postoperative seizures may also have been counted.

Many children who undergo FCD resective surgery can be successfully withdrawn from AEDs. Early drug tapering was not associated with a higher rate of seizure recurrence in the present study. Patients with FCD type IIb were more likely to remain seizure-free following AED reduction. In conclusion, if the postoperative pathology is FCD type IIb and no epileptic discharge is detected on the follow-up EEG, it is preferable to consider early AED tapering. Early AED tapering may be considered if the initial EEG obtained within 6 months of the surgery shows no definite epileptiform discharges. It is important to confirm these findings in a prospective, large-scale study.

Acknowledgments

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. The authors declare that there is no conflict of interest regarding the publication of this paper.

요약

목적: 본 연구는 소아 국소 겉질 형성이상 환자에서 뇌전증 수술 후 항경련제 복용 중단 성공과 관련된 요인들을 확인하고자 한다.

방법: 2003 년부터 2014 년 까지 세브란스 병원에서 국소 겉질 형성이상으로 수술적 제거술을 시행 받은 134명의 환자를 대상으로 후향적 의무기록 분석을 시행하였다. 항경련제 중단 과정에서 경련 재발을 경험한 환자군과 그렇지 않은 환자들의 성별, 뇌전증 발병 연령, 뇌전증 유병 기간, 국소 겉질 형성이상의 위치 및 조직병리학적 분류, 수술 후 항경련제 중단까지 걸린 시간 등을 분석하였다.

결과: 뇌전증 발병 평균 연령은 1.0 (IQR, 0.3-5.0)년이었다. 평균 추적 관찰 기간은 6.0 (IQR, 1.0-13.0)년 이었으며 총 134명 중 89명(66%)에서 항경련제 중단을 시작하였고 중단 후 28명(31%)에서 경련이 재발하였으며, 경련 재발 없이 지속된 경우는 61명(69%)이었다. 이 61명의 환자 중 38명(62%)이 모든 항경련제를 성공적으로 중단할 수 있

었다. 수술 후 항경련제 중단을 시작하기까지 걸린 기간은 3.5 (IQR, 0–90.1)개월이었고, 경련 재발 집단과 재발하지 않은 집단간에 의미 있는 차이는 없었다. 국소 겉질 형성이상 조직학적 분류 IIb 일때 항경련제 중단 후 경련 재발이 없을 가능성이 더 높았고(P=0.004), 뇌파 검사에서 경련파가 보이지 않을 때 경련 재발 가능성이 더 적게 나타났다(P=0.031).

결론: 국소 겉질 형성이상의 조직병리학적 분류와 뇌파 이상 소견을 통해 수술 후 성공적인 항경련제 중단 여부를 예측할 수 있다. 수술 후 항경련제 중단을 시작하는 시점이 빨라도 경련 재발률이 높아지지 않으므로, 수술 후 적극적으로 항경련제 중단을 고려 및 시작하는 것이 의미 있다.

References

1) Choi KO, Kang HC, Lee JS, Kim DS, Kim HD. Surgical outcomes and prognostic factors after epilepsy surgery in children with extratemporal lobe epilepsy. J Korean Child Neurol Soc 2010;18:20-32.
2) Wyllie E. Surgical treatment of epilepsy in pediatric patients. Can J Neurol Sci 2000;27:106-10.
3) Crino PB. Focal Cortical Dysplasia. Semin Neurol 2015;35:201-8.
4) Cole AJ, Wiebe S. Debate: Should antiepileptic drugs be stopped after successful epilepsy surgery? Epilepsia 2008;49 Suppl 9:29-34.
5) Practice parameter: a guideline for discontinuing antiepileptic drugs in seizure-free patients--summary statement. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 1996;47:600-2.
6) Ziemba KS, Wellik KE, Hoffman-Snyder C, Noe KH, Demaerschalk BM, Wingerchuk DM. Timing of antiepileptic drug withdrawal in adult epilepsy patients after neocortical surgical resection: a critically appraised topic. Neurologist 2011;17:176-8.
7) Ladino LD, Hernandez-Ronquillo L, Tellez-Zenteno JF. Management of antiepileptic drugs following epilepsy surgery: a meta-analysis. Epilepsy Res 2014;108:765-74.
8) Sinclair DB, Jurasek L, Wheatley M, Datta A, Gross D, Ahmed N, et al. Discontinuation of antiepileptic drugs after pediatric epilepsy surgery. Pediatr Neurol 2007;37:200-2.
9) Schiller Y, Cascino GD, So EL, Marsh WR. Discontinuation of antiepileptic drugs after successful epilepsy surgery. Neurology 2000;54:346-9.
10) Menon R, Rathore C, Sarma SP, Radhakrishnan K. Feasibility of antiepileptic drug withdrawal following extratemporal resective epilepsy surgery. Neurology 2012;79:770-6.
11) Lachhwani DK, Loddenkemper T, Holland KD, Kotagal P, Mascha E, Bingaman W, et al. Discontinuation of medications after successful epilepsy surgery in children. Pediatr Neurol 2008;38:340-4.
12) Tellez-Zenteno JF, Hernandez-Ronquillo L, Moien-Afshari F. Discontinuation of antiepileptic drugs after successful surgery: who and when? Epileptic Disord 2012;14:363-70.
13) Tellez-Zenteno JF, Ronquillo LH, Jette N, Burneo JG, Nguyen DK, Donner EJ, et al. Discontinuation of antiepileptic drugs after successful epilepsy surgery. a Canadian survey. Epilepsy Res 2012;102:23-33.
14) Tonini C, Beghi E, Berg AT, Bogliun G, Giordano L, Newton RW, et al. Predictors of epilepsy surgery outcome: a meta-analysis. Epilepsy Res 2004;62:75-87.
15) Hoppe C, Poepel A, Sassen R, Elger CE. Discontinuation of anticonvulsant medication after epilepsy surgery in children. Epilepsia 2006;47:580-3.
16) Schmidt D, Loscher W. Uncontrolled epilepsy following discontinuation of antiepileptic drugs in seizure-free patients: a review of current clinical experience. Acta Neurol Scand 2005;111:291-300.
17) Berg AT, Vickrey BG, Langfitt JT, Sperling MR, Shinnar S, Bazil C, et al. Reduction of AEDs in postsurgical patients who attain remission. Epilepsia 2006;47:64-71.
18) Boshuisen K, Arzimanoglou A, Cross JH, Uiterwaal CS, Polster T, van Nieuwenhuizen O, et al. Timing of antiepileptic drug withdrawal and long-term seizure outcome after paediatric epilepsy surgery (TimeToStop): a retrospective observational study. Lancet Neurol 2012;11:784-91.
19) Wilkins DE. A guideline for discontinuing antiepileptic drugs in seizure-free patients. Neurology 1999;53:239.
20) Park KI, Lee SK, Chu K, Jung KH, Bae EK, Kim JS, et al. Withdrawal of antiepileptic drugs after neocortical epilepsy surgery. Ann Neurol 2010;67:230-8.
21) Lee SY, Lee JY, Kim DW, Lee SK, Chung CK. Factors related to successful antiepileptic drug withdrawal after anterior temporal lobectomy for medial temporal lobe epilepsy. Seizure 2008;17:11-8.
22) Kim YD, Heo K, Park SC, Huh K, Chang JW, Choi JU, et al. Antiepileptic drug withdrawal after successful surgery for intractable temporal lobe epilepsy. Epilepsia 2005;46:251-7.