Clinical Neurology and Neurosurgery 144 (2016) 91–95

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Seizure outcome following medical treatment of mesial temporal lobe epilepsy: Clinical phenotypes and prognostic factors

Igor Kuzmanovski[a], Emilija Cvetkovska[a,*], Marija Babunovska[a], Gordana Kiteva Trencevska[a], Biljana Kuzmanovska[b], Bojan Boshkovski[a], Rozalinda Isjanovska[c]

[a] University Clinic of Neurology, Medical Faculty, Ss. Cyril and Methodius University, Vodnjanska str. 17, MK-1000, Skopje, Macedonia
[b] University Clinic of Intensive Care, Anaesthesiology and Reanimation, Medical Faculty, Ss. Cyril and Methodius University, Vodnjanska str, 17, MK-1000, Skopje, Macedonia
[c] Institute of Epidemiology and Statistics, Medical Faculty, Ss. Cyril and Methodius University, Vodnjanska str. 17, MK-1000, Skopje, Macedonia

ARTICLE INFO

Article history:
Received 26 November 2015
Received in revised form 20 February 2016
Accepted 8 March 2016
Available online 24 March 2016

Keywords:
Mesial temporal lobe epilepsy
Prognostic factors
Outcome

ABSTRACT

Objective: Surveys on mesial temporal lobe epilepsy (MTLE) repeatedly demonstrate that seizures are commonly resistant to antiepileptic drugs (AED), but patients usually came from third-level epilepsy centers, making the medically refractory population larger. The aim of our study is to evaluate patterns of seizure control and prognostic factors of general population of MTLE patients observed in clinical practice.

Methods: Sixty five MTLE patients were evaluated for demographic data, family history, febrile convulsions, detailed descriptions of auras and seizures, presence of secondarily generalized seizures, age at seizure onset, duration of epilepsy, epileptiform discharges in EEG, neuroradiological findings and AED schedules with therapeutic response. According to seizure frequency, patients were divided into three groups: (1) seizure-free (SF) patients at the time of evaluation, (2) patients considered as having infrequent seizures (IS) if they presented only auras or up to three dyscognitive (complex partial) seizures per year and (3) patients with higher rate were regarded as having frequent seizures i.e. being drug-resistant (DR). For each clinical parameter, the three groups were compared statistically. In addition, following the patterns of evolution over time, patients were categorized into two groups: continuous pattern, with no period of remission, and intermittent pattern, in which patients had at least one period of remission.

Results: Ten patients (15.4%) were seizure free, 19 (29.2%) had infrequent seizures, while 36 patients (55.4%) had frequent uncontrolled seizures. Ten (52.6%) IS patients and ten (27.7%) DR patients had a intermittent i.e. relapse-remitting pattern with at least one period of two years without seizures. Female patients dominated SF group and the gender difference with other groups reached statistical significance ($p = 0.02$). Comparing the groups, DR group had longer seizure duration than IS group (12.6 ± 10.9 years vs. 22.8 ± 10.6 years, $p = 0.006$). Number of tried AEDs ($p < 0.00006$) was significantly lower in the seizure-free patients. Other variables are not related to course of the epilepsy.

Conclusion: MTLE is a heterogeneous syndrome, 45% of patients in our series were having either rare auras or seizures or were seizure-free. The factors associated with drug resistance were longer duration of epilepsy, higher number of previously tried AED and male gender.

1. Introduction

Mesial temporal lobe epilepsy (MTLE) is the most common form of partial epilepsy in adults [1]. The typical seizures include autonomic and/or psychic aura, alteration of consciousness, gestural and oral-alimentary automatisms, dystonic posturing and prolonged postictal reorientation [2]. The clinical history of MTLE sometimes reveal an early initial injury: febrile convulsions, central nervous system (CNS) infections or head injury, followed by a latent period, before chronic epilepsy develops [3]. The seizures are often resistant to antiepileptic drugs [1], although clinical phenotypes who achieve long seizure-free periods with antiepileptic drugs (AED) has been described [4,5]. Hippocampal sclerosis (HS) is the most common pathology in MTLE, and medically refractory

* Corresponding author.
E-mail address: emilicvetkovska@gmail.com (E. Cvetkovska).

http://dx.doi.org/10.1016/j.clineuro.2016.03.018
0303-8467/

Table 1
Demographic, clinical and neuroradiologic factors of the patients.

		Group 1 n = 10		Group 2 n = 19		Group 3 n = 36		Total n	p-Value
		Seizure free		Infrequent seizures		Drug-resistant			
		N	%	N	%	N	%		
Gender	M	0	0	9	47.6	20	44.4	29	**p = 0.024**
	F	10	100	10	52.6	16	55.6	36	
Family history	No	5	50	11	57.9	27	75	43	p = 0.223
	Yes	5	50	8	42.1	9	25	22	
Febrile seizures	No	8	80	15	78.9	30	83.3	53	p = 0.809
	Yes	2	20	4	20	6	16.1	12	
Generalized seizures	No	8	80	3	16.1	7	19	18	p = 0.937
	Yes	2	20	16	84.2	29	80.6	47	
Hyppocampal sclerosis	No	8	80	8	57.9	23	63.9	39	p = 0.109
	Yes	2	20	11	42.1	13	36.1	26	

Bold values are statistically significant (p < 0.05).

patients are treated successfully by temporal lobe resection [6]. An early onset of epilepsy, history of febrile convulsions, interictal epileptiform activity on electroencephalogram (EEG), duration of epilepsy, response to the first antiepileptic drug, number of seizures per month before treatment, HS, age of traumatic brain injury (TBI), presence of mental retardation and female gender are found to be prognostic factors in number of studies on MTLE [7–9].

Although great improvement has been achieved in understanding the natural history of MTLEs in the last decades, one of the limitations of previous studies is that a large number of patients came from third-level epilepsy centers, making the drug resistant population larger. The aim of our study is to evaluate patterns of seizure control and prognostic factors of general population of MTLE patients observed in clinical practice.

2. Methods

We evaluated 65 patients with MTLE treated medically at Epilepsy Department, University Clinic of Neurology in Skopje, which is referral center for patients with epilepsy for the entire country. Patients were selected according to the following inclusion criteria:

1. Typical clinical description of mesial temporal lobe seizures (usually with auras that consisted of epigastric, autonomic, and/or psychic sensations followed by an arrest of motor activity, progressive loss of consciousness, and automatisms of the mouth and hands, with or without secondary generalisation);
2. Interictal or ictal electroencephalographic (EEG) epileptiform abnormalities over temporal or frontotemporal regions;
3. MRI findings: either the presence of atrophy and increased hippocampal signal (MTLE associated with HS) or normal MRI (non-lesional MTLE). Patients with MTLE of other etiologies (tumor, vascular or cortical malformations) were not selected.

Possible candidates were identified by retrospectively reviewing all clinical records from our database. All candidates with at least one year of follow-up were invited for reevaluation visit, standardized forms were filled out and if needed and additional tests were done. All patients signed Informed Consent approved by the Ethics Committee of Medical Faculty in Skopje. The data for each patient included demography (age and gender), complete family history, potential antecedent events such as perinatal asphyxia, severe head injury, CNS infection or febrile convulsions, detailed descriptions of auras and seizures, presence of secondarily generalized seizures, age at seizure onset, duration of epilepsy, duration of follow-up, epileptiform discharges in EEG and neuroradiological findings. Age at seizure onset refers to age at onset of habitual seizures, excluding febrile seizures. The duration of epilepsy was defined as the interval between the age at onset of habitual seizures and the time when this evaluation was performed.

Every patient underwent repeated EEG recordings during wakefulness and, when possible, during diurnal sleep induced by sleep deprivation. Twenty digital channels were used, following the international standards requiring the placement of 10–20 electrodes, with additional T1, T2 electrodes. In 12 patients, ictal recordings during video EEG monitoring was acquired. MRI images using 1.5 T scanners (coronal T1-IR, T2 and FLAIR; axial T2) were obtained in all patients. Particular attention was paid on AED schedules with extensive evaluation of therapeutic response over time. The long-term seizure control of each patient was assessed from the seizure onset period. According to the frequency of seizures, patients were divided into three groups. The first group included patients who were seizure-free (SF) at the time of evaluation. Seizure freedom was defined as a period without seizures for a minimum of three times the longest preintervention interseizure interval (determined from seizures occurring within the past 12 months) or 12 months, whichever is longer [10]. The second group included patients considered as having infrequent seizures (IS) if they presented only auras or up to three dyscognitive (complex partial) seizures per year and no generalized tonic-clonic seizures (GTCS). Patients with higher rate were regarded as having frequent seizures i.e. being drug-resistant (DR). For each clinical parameter, the three groups were compared statistically. In addition, following the patterns of evolution over time, patients were categorized into two groups: continuous pattern, with no period of remission, and

Table 2
The effect of specific parameters on prognosis.

	Group 1 n = 10 Seizure free Mean ± SD	Group 2 n = 9 Infrequent seizures Mean ± SD	Group 3 n = 36 Drug-resistant Mean ± SD	p-Value
Average duration (year)	14.3 ± 15.93	12.6 ± 10.9	22.8 ± 10.5	0.006
Age at onset (year)	15.6 ± 8.1	19.6 ± 15.6	15.4 ± 11.1	0.46