

Is It True Refractory Epilepsy or Not? Follow up of Patients in Tertiary Epilepsy Unit

Gerçek Dirençli Epilepsi Mi? Üçüncü Basamak Merkezde Hastaların Takibi

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Abstract

Early recognition of refractory epilepsy is so important to apply alternative therapeutic approach to the patient. However, misdiagnosis of refractory epilepsy is common. Pseudo-Refractory epilepsy is defined as seizures inadequately treated due to incorrect diagnosis, use of incorrect and/or low dose antiepileptic drug (AED) and poor compliance of patients. The aim of the present paper was to investigate the patients with true and pseudo-refractory epilepsy. The files of four hundred and forty-nine patients (March 2014-January 2017) reviewed by the same neurologist retrospectively and the patients with true and pseudo-refractory epilepsy were determined. Seventy-eight (66.1%) of the patients was with true refractory epilepsy. Fourteen (11.9%) patients had misdiagnosis; twelve (10.2%) patients used inappropriate medicine; eleven (9.3%) patients was treated with inadequate dose of antiepileptic drug; three patients had poor compliance of treatment received monotherapy. Differentiation of pseudo-refractory and true refractory epilepsy are very important for avoiding unnecessary treatment approaches and future management of true refractory epilepsy.

Keywords: Epilepsy, Intractable Epilepsy, Pseudo Refractory Epilepsy

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Introduction

Drug resistant epilepsy is defined as failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom (1). Early recognition of drug resistant epilepsy is so important to apply alternative therapeutic approach to the patient including respective surgery, ketogenic diet and vagal nerve stimulation. Misdiagnosis of refractory epilepsy is common (2). Pseudo-Refractory epilepsy is defined as seizures inadequately treated due to incorrect diagnosis, use of incorrect and/or low dose antiepileptic drug (AED) and poor compliance of patients (3). The aim of the present paper was to investigate the patients with true and pseudo-refractory epilepsy.

Material and Method

The files of four hundred and forty-nine patients (March 2014-January 2017) were reviewed by the same neurologist retrospectively and the patients

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Öz

Refrakter Epilepsinin erken tanısı, alternatif tedavi yaklaşımlarını uygulamak için çok önemlidir. Bununla beraber, refrakter epilepsinin yanlış tanısı siktir. Yalancı-Refrakter Epilepsi yanlış tanı, yanlış ve/veya düşük doz antiepileptik ilaç kullanımı ve hastanın kötü uyumuna bağlı nöbet kontrolündeki yetersizliktir. Bu çalışmanın amacı, gerçek ve yalancı refrakter epilepsi hastalarını incelemektir. Dört yüz kırk dokuz hastanın dosyaları (Mart 2014-Ocak 2017) aynı nörolog tarafından geriye dönük olarak incelenmiştir ve gerçek refrakter ve yalancı refrakter epilepsi hastaları saptanmıştır. Yetmiş sekiz (%66.1) hastada gerçek refrakter epilepsi tespit edilmiştir. On dört (%11.9) hastada yanlış tanı mevcuttu; on iki (%10.2) hastada uygun olmayan tedavi alıyordu; onbir hasta (%9.3) yetersiz dozda antiepileptik ilaç kullanıyordu, monoterapi alan üç hastada yetersiz tedavi uyumuna sahipti. Gerçek ve yalancı refrakter epilepsinin ayırıcı tanısı yetersiz tedavi yaklaşımlarında ve gerçek refrakter epilepsinin gelecek tedavisinde çok önemlidir.

Anahtar Kelimeler: Dirençli Epilepsi, Epilepsi, Yalancı Refrakter Epilepsi

with true and pseudo-refractory epilepsy were determined. The patients who had not enough control of seizures despite at least two different AED regimens before being admitted to our department and had no seizure at least one year after the revision of the diagnosis and/or treatment of epilepsy in our epilepsy department, were accepted as the patients with pseudo-refractory epilepsy. Demographic data, medical and epilepsy history, seizure type and frequency, routine EEG, neuroimaging findings were collected in all patients. Long term video-EEG monitoring, home video recording and cardiology consultation were also investigated in patients who had doubt in the diagnosis of epilepsy.

Results

One hundred eighteen patients out of four hundred and forty-nine patients were determined with refractory epilepsy; fifty-five (46.6%) of whom were male and sixty-three (53.4%) of whom were female. Ninety-seven (82.2%) patients took polytherapy and twenty-one (17.8%) received monotherapy. Seventy-eight (66.1%) of the patients were with true refractory epilepsy. Table 1 shows causes of resistance in patients with intractable epilepsy.

Misdiagnosis of epilepsy was observed in 14 (11.9%) patients. Thirteen of them had psychogenic

non-epileptic seizures (PNES), one of them had paroxysmal kinesigenic dyskinesia. Long term video-EEG monitoring was used to make a diagnosis in 8 patients. PNES was diagnosed in three patients by home video recording. The EEGs of these patients with misdiagnosis were normal except one patient. Psychiatry consultation was applied to thirteen patients. After this consultation, the antiepileptic drugs (AED) were stopped and/or the dosage of AED was decreased. Seizure control of these patients was achieved in follow up period (6-45 months). The treatment of patient with paroxysmal kinesigenic dyskinesia was changed from levetiracetam 3000 mg/day to carbamazepine 400 mg/day. After that, no dyskinesia was observed (follow up period: 38 months).

Table 1. Causes of resistance in patients with intractable epilepsy

Cause of resistance	Number of patients
True refractory epilepsy	78 (66.1%)
Misdiagnosis	14 (11.9%)
Inappropriate medicine	12 (10.2%)
Inadequate dose of antiepileptic drug	11 (9.3%)
Poor compliance of treatment	3 (2.5%)

An incorrect diagnosis of seizure classification that led to incorrect drug choice was observed in eleven patients. Idiopathic generalized epilepsy syndromes especially juvenile myoclonic epilepsy and juvenile absence epilepsy were unrecognized and inappropriately treated with narrow spectrum AEDs (e.g carbamazepine) in these patients. These patients were seizure free after the suitable AED usages at least six month follow up (follow up period: 6-44 months).

Inadequate dosing of AED was seen in eleven (9.3%) patients. All of them were under polytherapy. Complete seizure control was achieved after the regulation of AEDs (follow up period: 6-40 months) Noncompliance with AED and inappropriate life style were determined in three (2.5%) patients. These patients were supported by family members and friends in addition to a good doctor-patient relationship. Precipitating factors for seizures were explained to the patients. All patients were seizure free after good compliance, regulation of life style and AED treatment (follow up period: 6-32 months).

Discussion

Patients with epilepsy whose seizures do not successfully respond to antiepileptic drug (AED) therapy are considered to have drug-resistant epilepsy (4-5). When a patient's seizures do not respond to antiepileptic drug (AED) therapy; the clinician should reconsider the seizure classification and the appropriateness of the AED that have been employed. The diagnosis of epilepsy should also be considered. Therefore, it is important to differentiate true versus pseudo refractory epilepsy. Detailed seizure and epilepsy history, induction of seizure during routine EEG, home video camera recording and psychiatric evaluation were helpful in the diagnosis of true refractory-pseudo refractory epilepsy. Psychogenic non-epileptic seizure (PNES) can mimic epileptic seizures. PNES usually do not respond to AED therapy. 25-40% of the patients who were referred to epilepsy center were diagnosed as PNES (6-7). In addition to PNES, other non-epileptic paroxysmal events, especially syncope but also certain sleep and movement disorders, can be mistaken for epilepsy (2,8). In our study fourteen (11.9%) patients had misdiagnosis; one of them diagnosed with paroxysmal kinesigenic dyskinesia; and the others with PNES.

An incorrect diagnosis of seizure classification led to incorrect drug choice. It is not uncommon for idiopathic generalized epilepsy syndromes to be unrecognized and inappropriately treated with narrow spectrum AEDs (9). In other cases, inadequate dosing or frequency of AED dosing has led to apparent intractability (2). In our study twelve (10.2%) patients used inappropriate medicine; eleven (9.3%) patients were treated with inadequate dose of antiepileptic drug. Noncompliance with AED is a common problem. In one case series, 71% of patients reported at least occasional dose omissions, and 45 percent reported a seizure after a missed dose (10). Support from family members and physicians increase medical compliance (9,11-12). Some factors about lifestyle of patients including alcohol and sleep deprivation may also increase seizure frequency (9, 12-13). We found that three (2.5%) patients had poor compliance of treatment. Pseudo-refractory patients are still a big problem in our clinical practice. Differentiation of pseudo-refractory and true refractory epilepsy are very important for avoiding unnecessary treatment approaches and future management of true refractory epilepsy.

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