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Effect of treating helicobacter pylori infection on seizure frequency in patients with refractory epilepsy

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Ali Akbar Asadi-Pooya[1], Seyed Mohsen Dehghani[2], Mehrdad Emami[3]

[1]Associate Professor, Department of Neurology, Shiraz University of Medical Sciences, Shiraz, Iran AND Adjunct Research Assistant Professor, Department of Neurology, Thomas Jefferson University, Philadelphia, USA
[2] Associate Professor of Pediatric Gastroenterology, Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[3] Shiraz University of Medical Sciences, Shiraz, Iran

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Refractory Epilepsy, Seizure Frequency, Helicobacter Pylori

Abstract

Background: The main purpose of the current study was to determine the effect of treating helicobacter pylori (HP) infection on seizure frequency in patients with refractory epilepsy.

Methods: A small sample of adult patients above 18 years of age with a diagnosis of refractory epilepsy was studied at the outpatient epilepsy clinic at Shiraz University of Medical Sciences, from January 2009 through June 2011. If and when urea breath test result was positive, an upper endoscopy with multiple gastric biopsies was requested. Rapid urease test and histopathology examination were performed. For patients with confirmed HP infection, treatment with clarithromycin, amoxicillin and omeprazole was ordered for two weeks. Seizure frequency was recorded before and after HP treatment.

Results: Nine patients were recruited. Using Wilcoxon signed ranks test, seizure frequency did not differ significantly after HP treatment compared to the period before treatment (P = 0.6).

Conclusion: Treating HP infection in patients with refractory epilepsy did not significantly change the seizure frequency.

Introduction

Drug resistant epilepsy is an epilepsy syndrome or disorder in which seizures persist and seizure freedom is very unlikely to be attained with further manipulation of antiepileptic drug (AED) therapy. It is defined as failure of adequate trials of two tolerated, appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.[1] Drug resistance is thought to be common among patients with epilepsy. Two major neurobiological mechanisms of drug resistant epilepsy are supposed to be removal of AEDs from the epileptogenic neurons and glia through excessive expression of multi-drug efflux transporters such as P-glycoprotein and reduced drug target sensitivity in epileptogenic brain tissue.[2]

The probable role of helicobacter pylori (HP) infection in extra-intestinal diseases has been investigated and suggested in previous studies.[3-5] It has been suggested that HP might influence the pathophysiology and therefore the management of seizures in epilepsy.[6] However, there are contradictory results with regard to the association between HP infection and epilepsy in the literature.[3,4,7] This contradiction implies the need for further well-designed studies to investigate the relationship between HP infection and epilepsy, particularly in patients with refractory seizures. The main purpose of the current study was to determine the effect of treating HP infection on seizure frequency in patients with refractory epilepsy infected with this micro-organism.

Corresponding Author: Ali Akbar Asadi-Pooya.
Associate Professor, Department of Neurology, Shiraz University of Medical Sciences, Shiraz, Iran AND Adjunct Research Assistant Professor, Department of Neurology, Thomas Jefferson University, Philadelphia, USA
Email: aliasadipooya@yahoo.com

Materials and Methods

Patients above 18 years of age with a diagnosis of idiopathic generalized epilepsy (IGE) or temporal lobe epilepsy (TLE) with refractory seizures[1] were recruited at the outpatient epilepsy clinic at Shiraz University of Medical Sciences, from 2009 through 2011. Patients with IGE had typical seizures (e.g., absences, myoclonic jerks or generalized tonic-clonic seizures) and typical signs in the electroencephalograms (e.g., spike-wave complexes and/or polyspikes). Patients with TLE had also typical seizures (e.g., simple partial seizures, complex partial seizures, or secondary generalized tonic-clonic seizures) and signs in the electroencephalograms (e.g., temporal epileptiform discharges).

For all patients a urea breath test (UBT) was requested. No one took any drug with possible interactions with UBT (e.g., omeprazole, metronidazole, etc.). If and when UBT result was positive, an upper endoscopy with multiple gastric biopsies was requested. Rapid urease test and histopathology examination were performed on all the samples. Patients with confirmed HP infection were recruited in the final stage of the study and treatment with clarithromycin, amoxicillin and omeprazole was ordered for two weeks.

Seizure frequency was recorded in two time periods; the first period, starting from two months before HP treatment initiation until the day HP treatment started and the second period starting from the day after HP treatment completed (for two weeks) until two months later. AED regimen was not changed during the study period.

Statistical analyses were performed using Wilcoxon signed ranks test to determine potentially significant differences and a P-value less than 0.05 was considered significant. Vice chancellor for research in Shiraz University of Medical Sciences approved this study. Informed consent was obtained from all the patients.

Results

Two patients with IGE and seven patients with TLE were recruited in the study. Among patients with IGE, one patient was female and the other one was male. Among patients with TLE, all were female. Their mean age was 33 ± 8 years.

Seizure frequency among the patients, before and after HP treatment is presented in table 1. In four patients seizure frequency after HP treatment was less compared with the time period before treatment. In three patients, seizure frequency after HP treatment was more compared with the time period before treatment. In two patients, seizure frequency did not change. Using Wilcoxon signed ranks test, seizure frequency did not differ significantly after HP treatment compared to the time period before treatment (P = 0.6).

Table 1. Seizure frequency among patients, before and after helicobacter pylori treatment

Seizure frequency	Before treatment (number of patients)	After treatment (number of patients)
1 per 2 months	2	0
1 per month	2	2
2 per month	3	1
3 per month	0	3
4 per month	1	1
6 per month	1	0
Mean seizure frequency per month ± standard deviation	2.2 ± 1.8	1.9 ± 1.5

In a 22-year-old female with IGE, seizure frequency prior to HP treatment was 1 per 2 months and after treatment the seizures were controlled for six months, before they recurred. In a 35-year-old female with TLE, seizure frequency prior to HP treatment was 1 per month and after treatment the seizures were controlled for two months, before they recurred.

Discussion

The mechanisms underlying the refractory epilepsy are not well understood. Unidentified or unknown causes are probably responsible for some cases of drug resistant epilepsies. Searching for these possible etiologies may help understand and manage these patients more successfully. The relationship between HP infection and some extra-intestinal diseases has been studied and documented before.[3-5] This relationship is probably associated with immunological mechanisms.[6] In previous studies, it has been observed that HP infection was more frequent in patients with epilepsy compared to healthy control[3] and patients with other chronic disorders.[4]

However, in a recent study, we observed that the rate of HP infection was not higher in patients with epilepsy compared to healthy control.[7] In the current study, we observed that treating HP infection in patients with refractory epilepsy did not significantly change the seizure frequency. Even in that minority of patients with a substantial change and cessation of seizures, the effect was not long-lasting and seizures recurred after a short period of time.

Limitation of the study

The small sample size of this study was a barrier to make any extrapolation and more well-designed studies are required in order to reach a final conclusion with regard to the role of HP infection in epilepsy.

Conclusion

We observed that treating HP infection in patients with refractory epilepsy did not significantly change the seizure

frequency and we believe that at the moment there is not enough data to support the role of HP infection in refractoriness of the seizures in patients with epilepsy.

Acknowledgment

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Conflict of interest

The authors have no conflict of interest.

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