Review

A Review on Epilepsy and Planned Pregnancy

in Patients with Epilepsy

Burak Bayrak^{1*} Busra Yuksel¹ Yucel Kadıoglu¹

¹Department of Analytical Chemistry, Faculty of Pharmacy, Ataturk University, 25240

ABSTRACT:

The number of patients with epilepsy varies regionally around the world, but it is one of the most common neurological diseases. The treatment and diagnosis of epilepsy is a complex condition. The term "resolved" is used in the treatment of epilepsy. When the epilepsy is resolved, it means that the person no longer has epilepsy, but it does not guarantee that it will not return. When the disease reaches certain ages, it can improve without treatment. In patients with epilepsy, pregnancy is possible, but the treatment to be applied in terms of maternal and child health should be chosen correctly. If reliable drugs are chosen in terms of teratogenicity in the treatment of epilepsy in pregnancy and pregnancy is planned, patients can become mothers with confidence. In this review, information about epilepsy disease, historical prevalence of the disease and drugs that are safe to use in patients with epilepsy are given.

Keywords: Antiepileptic drugs, epilepsy, pregnancy

Received	Accepted	Published	
20.08.2021	25.09.2021	15.10.2021	

To cite this article:

Bayrak B, Yuksel B, Kadıoglu Y. A review on epilepsy and planned pregnancy in patients with epilepsy. International Journal of PharmATA. 2021; 1(1); 33-37.

1. INTRODUCTION

Epilepsy is one of the oldest diseases with written records dating back to 4000 BC. It is a chronic disease, also known as "sara" disease among the turkish people. Epilepsy can be characterized as "the predisposition of the brain to produce epileptic seizures with neurobiological, cognitive, psychological and social consequences". About 50 million people worldwide are thought to have epilepsy, and this makes it one of the most common neurological diseases worldwide [1]. An estimated five million people are diagnosed with epilepsy each year [1]. In the study conducted between 1990 and 2016, which calculated the burden of worldwide, global and regional neurological diseases, it was shown that epilepsy is the 5th most common disease worldwide, and It is also one of the most common (2-8) diseases in the regionally. (Figure.1) [2].

* Corresponding Author:			+90 4422315425 Department of Analytical Chemistry, Faculty of Pharmacy, Ataturk University, 25240, Erzurum, Turkey
	E-mail	:	burak.bayrak@atauni.edu.tr 33

Considering the estimated rates around the world, this number is estimated to be around 600 thousand in our country, but no official figures have been reached on this subject. Epilepsy is a disease that affects people of all ages, races, social classes and geographical locations. The worldwide incidence and prevalence of epilepsy is slightly higher in men than in women [3]. The reason for this difference can be shown as hiding the disease of women due to socio-cultural reasons in various cultures [4]. Patients with epilepsy suffer from social problems such as stigma, exclusion, restrictions, overprotection and isolation, as well as seizures of epileptic disease.

Rank -5 -10 -15	Global	East Asia	Southeast Asia	Oceania	Central Asia	Central Europe	Eastern Europe	High-income Asia Pacific	Australasia	Western Europe	Southern Latin America	High-income North America	Caribbean	Andean Latin America	Central Latin America	Tropical Latin America	North Africa and Middle East	South Asia	Central sub-Saharan Africa	Eastern sub-Saharan Africa	Southern sub-Saharan Africa	Western sub-Saharan Africa
Stroke																			1			
Migraine		3	3	3												3			4	3	3	3
Alzheimer's disease and other dementias	3				4	3	3	3	3	3	3	3	3	3	3		3	4	3	4	4	4
Meningitis	4	11	5	4	9	12	10		13	13	11	13	4	9	10	8	5	3			5	2
Epilepsy	5	5	4	5	3	7	8	6	7	6	5	6	5	4	4	4	-4	6	5	5		5
Spinal cord injury	6	7	8	9	7	6	5	4	4	4	4	4	9	8	9	9	6	9	6	7	10	9
Traumatic brain injury	7	6	6	7	5	4	4	7	8	8	9	8	7	7	6	7	9	7	7	8	6	7
Brain and other CNS cancer	8	4	9	10	6	5	6	8	5	5	6	5	8	6	7	5	8	10	9	11	9	10
Tension-type headache	9	8	10	8	10	8	7	5	6	7	7	7	6	5	5	6	7	8	8	9	7	6
Encephalitis	10	9	7	6	8	13	11	11			12		11	10	11	12	10	5	10	10	11	8
Parkinson's disease	11	10	11	12	12	9	9	10	9	10	8	9	12	11	12	11	12	13	13	13	12	13
Other neurological disorders	12	12	12	11	11	10	12	9	10	9	10	10	10	12	8	10	11	12	12	12	8	12
Tetanus	13		13	14									13					11	11	6		11
Multiple sclerosis		14			13	11	13	13	12	11	13	11					13		14	14	13	
Motor neuron diseases		13		13	14			12	11	12		12		13	13	13					14	

Figure 1. Ranking of epilepsy in neurologic diseases according to different regions [2]

Observations made by W. Allen Hauser et al. in the USA between 1935 and 1984 showed that the prevalence of epilepsy was 86 per 100,000 during childhood (first years of life), while it decreased to 23-31 per 100,000 at the age of 30-60, this rate increases up to 180 per 100,000 in the advancing age group, that is, in the group over the age of 85. that is, an increased incidence of epilepsy is observed in the youngest and older groups [5].

Features that define an epileptic syndrome include family history, age of onset, presumed etiology, EEG (electroencephalography) and neuroimaging findings [6]. Family history and EEG observations are considered the most important tools in the evaluation of epilepsy patients [7]. However, due to the stress in the family at the time of the seizure, the events cannot be accurately conveyed when taking the family history, problems may arise because the diagnosis is partially based on remembered family and patient information.

Apart from the difficulties in reaching clinical diagnoses, the physician's lack of knowledge and training to diagnose specific epilepsy is also an important problem. The diagnosis and treatment of the patient's epilepsy should be decided in consultation with the specialist in the management of epileptic seizures. In the study by Leach et al. in the United Kingdom, to showed that in addition to adequate findings in the diagnosis of epilepsy, the importance of the physician who made the diagnosis is great. In a comparison between neurologists and non-specialist physicians, the rate of misdiagnosis was found to be 5.6% versus 18.9%, respectively [8]. It is not possible to avoid misdiagnosis, but with appropriately trained doctors, the probability of epilepsy being misdiagnosed can be kept lower.

Remission, a medical term for the absence of disease activity, is used to treat epilepsy. However, due to the difficulty in understanding the word by the public, experts suggested using the term "resolved" [9]. Epilepsy is not necessarily lifelong and is considered resolved if a person has not had a seizure for the past 10 years, has taken a break from seizure medication for at least the past 5 years, or is over one year old [10]. When the epilepsy is resolved, it means that the person no longer has epilepsy, but it does not guarantee that it will not return. In addition, when the patient reaches certain ages, it may improve and may not need treatment. In these cases, the physician's decision about what to do is important.

The percentage of untreated patients to the total number of patients with active epilepsy is called the "treatment gap" [11]. The 'treatment gap' ranges from 10 percent in developed countries to 75 percent in low-income countries [12]. This shows that three out of every four patients in low-income countries do not receive the necessary treatment, and this rate even goes up to 90% in some countries [1].

Epilepsy treatment should begin with monotherapy. Antiepileptic drug (AED) monotherapy remains the most appropriate approach for the treatment of most patients with epilepsy (except when the patient is experiencing more than one type of epilepsy) [13]. The main reason for recommending monotherapy is that it is treated with a single drug to reduce side effects and toxicity, as the drugs used have various side effects, ranging from minor deterioration in the CNS to liver failure and even suicide [14]. When patients fail monotherapy, initiation of a new AED monotherapy, initiation of AED polytherapy, or various non-pharmacological (epilepsy surgery, vagus nerve stimulation, ketogenic diet, reactive neurostimulation) treatments may also be administered. Apart from these, complementary and alternative therapies such as acupuncture, traditional Chinese medicine, cannabinoids, melatonin, vitamin supplement and yoga have been researched, but there is no evidence for their efficacy in treatment [15].

1.1. Epilepsy and Pregnancy

AED has many teratogenic effects, especially congenital heart defects, neural tube defects, cleft lip and cleft palate. Treatment reaching toxic levels or undesirable side effects caused by multi-drug therapy should be avoided. Although it has been shown that new generation AEDs are partially better in terms of teratogenicity, they lead to unsuccessful results in terms of seizure control, which leads to polytherapy or dose increase and an increased risk of teratogenicity [16]. As a

result of studies on the safety of AEDs used during pregnancy, levetiracetam, oxcarbazepine and lamotrigine were reported to be the least risky drugs [17-21]. Although it has low risk, drug monitoring and dose adjustment may be required during pregnancy in pregnant women taking lamotrigine and oxcarbazepine [22].

2.1. CONCLUSION

Although pregnancy is risky in patients with epilepsy, patients who plan to have children should be informed that they can have an uneventful pregnancy and have children. The most important condition for this is to plan the pregnancy. In an epileptic patient who wants to become pregnant, it is recommended to discontinue the drug or drugs used as the first choice, if possible, and to apply monotherapy, in which drug levels are carefully controlled, as a second option. In a planned pregnancy, monotherapy should be applied before fertilization occurs when the dosage of the drug is high enough to control seizures and low enough not to harm fetal development. that is, the lowest effective dose should be treated.

Conflict of Interest

Author has no personal financial or non-financial interests.

REFERENCES

1.World Health Organization. Epilepsy. 2019;20:6. Accessed 1 September 2021. Available: http://www.globalizationandhealth.com/content/1/1/14.

2. Feigin VL, Nichols E, Alam T, Bannick MS, Beghi E, Blake N, et al. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology. 2019;18(5):459-480.

3. Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, et al. Prevalence and incidence of epilepsy: a systematic review and meta-analysis of international studies. Neurology. 2017;88(3):296-303.

4. Bharucha NE, Bharucha EP, Bharucha AE, Bhise AV, Schoenberg BS. Prevalence of epilepsy in the Parsi community of Bombay. Epilepsia. 1988;29(2):111-5.

5. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935–1984. Epilepsia. 1993;34(3):453-458.

6. Proposal for Revised Classification of Epilepsies and Epileptic Syndromes. Commission on classification and terminology of the International League Against Epilepsy. Epilepsia. 1989;30(4):389-399.

7. Hampel KG, Garcés Sánchez M, Gómez Ibañez A, Palanca-Cámara M, Villanueva V. Desafíos diagnósticos en epilepsia. Rev Neurol. 2019;68(6):255-263.

8. Leach, J. Lauder R.. Nicolson A. Smith D. Epilepsy in the UK: Misdiagnosis, mistreatment, and undertreatment?: The Wrexham area epilepsy project. Seizure. 2005;14(7):514-520.

9. Villanueva, V. Sanchez-Alvarez J.. Pena P. Salas-Puig J. Caballero-Martinez F. Gil-Nagel A. Treatment initiation in epilepsy: an expert consensus in Spain. Epilepsy & Behavior. 2010;19(3):332-342.

10. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475-482.

11. Meinardi H, Scott R, Reis JS. On Behalf Of The Ilae Commission on the Developing World. The treatment gap in epilepsy: the current situation and ways forward. Epilepsia. 2001;42(1):136-149.

12. Meyer, A, Dua CT, Ma J, Saxena S, Birbeck G. Global disparities in the epilepsy treatment gap: a systematic review. Bulletin of the World Health Organization. 2010;88:260-266.

13. St Louis EK, Rosenfeld WE, Bramley T. Antiepileptic drug monotherapy: the initial approach in epilepsy management. Current neuropharmacology. 2009;7(2):77-82.

14. Brunton LL, Hilal-Dandan R, Knollmann BC. Goodman & Gilman's the pharmacological basis of therapeutics. 2018: McGraw-Hill Education New York.

15. Liu G, Slater N, Perkins A. Epilepsy: treatment options. American family physician. 2017;96(2):87-96.

16. Vajda FJ, Hitchcock A, Graham J, O'Brien T, Lander C, Eadie M. Seizure control in antiepileptic drug-treated pregnancy. Epilepsia. 2008;49(1):172-176.

17. Canger R, Battino D, Canevini MP, Fumarola C, Guidolin L, Vignoli A, et al. Malformations in offspring of women with epilepsy: a prospective study. Epilepsia. 1999;40(9):1231-6.

18. MacDonald SC, Bateman BT, McElrath TF, Hernández-Díaz S. Mortality and morbidity during delivery hospitalization among pregnant women with epilepsy in the United States. JAMA neurology. 2015;72(9):981-988.

19. Morrow J, Russell A, Guthrie E, Parsons L, Robertson I, Waddell R, et al. Malformation risks of antiepileptic drugs in pregnancy: a prospective study from the UK Epilepsy and Pregnancy Register. Journal of Neurology, Neurosurgery & Psychiatry. 2006;77(2):193-198.

20. Moore JL, Aggarwal P. Lamotrigine use in pregnancy. Expert opinion on pharmacotherapy. 2012;13(8):1213-1216.

21. Holmes LB, Hernandez-Diaz S. Newer anticonvulsants: lamotrigine, topiramate and gabapentin. Birth Defects Research Part A: Clinical and Molecular Teratology. 2012;94(8):599-606.

22. Group ES. Seizure control and treatment in pregnancy: observations from the EURAP epilepsy pregnancy registry. Neurology. 2006;66(3):354-360.