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ORIGINAL ARTICLE

Pregnancy and Epilepsy: Clinical Data and Adverse Outcomes of Pregnant Women with Epilepsy

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Abstract

Objectives: Pregnancy in women with epilepsy carries a higher risk for fetal development complications, including congenital malformations. In this study, data obtained from pregnant epilepsy patients in a tertiary epilepsy center were presented.

Methods: In this study, 128 pregnancies of 110 pregnant women followed up in the epilepsy outpatient clinic between April 2011 and April 2021 were examined. Demographic data of the patients, antiepileptic drugs AEDs used, and pregnancy outcomes were reviewed retrospectively.

Results: During pregnancy, 101 patients (78.9%) received monotherapy, and lamotrigine was the most commonly used drug in monotherapy. A two-drug combination was used in 18 patients (14.1%), and a three-drug combination was used in 5 patients (3.9%). Although the frequency of seizures did not increase in most patients, the frequency of seizures increased in 18 patients (14.1%) and decreased in 5 patients (3.9%). In our study, the intrauterine fetal loss occurred in five patients, newborn infants with congenital malformations in three patients, and neonatal death during delivery in one patient. The number of AEDs used in multivariate logistic regression predicted adverse outcomes such as intrauterine fetal loss, neonatal death, and newborns with congenital malformations.

Conclusion: Management of pregnant patients with epilepsy is difficult for both mother and fetus. In our study, combination therapy was more associated with adverse outcomes for the fetus and newborn. Pregnancy should be planned, and seizure-free pregnancy should be targeted with low-dose monotherapy.

Keywords: Antiepileptic drugs; epilepsy; fetal malformation; pregnancy.

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Introduction

Epilepsy is a chronic neurological disease that may require long-term or lifelong treatment and is caused by the increased excitability of nerve cells in the brain. Recurrent seizures characterize it, but it causes serious problems in the individual's emotional, psychological, intellectual, and social functions.[1,2] Pregnancy causes both physiological and psychological changes in the individual. The coexistence of pregnancy and epilepsy is a more complex situation. Approximately 1/3 of women with epilepsy are of childbearing age, 3–5/1000 of total births occur in women with epilepsy.[3] It was observed that approximately half of the pregnant women with epilepsy did not have seizures during pregnancy. However, one-third of women also have increased seizure activity during pregnancy.[4,5]

Maternal and infant mortality rates, pregnancy, and birth complications are more common in epilepsy patients during pregnancy than in the normal population.[6] Both epileptic seizures and antiepileptic drugs AEDs used during pregnancy have important short- and long-term effects on maternal and fetal health. Which AED is safer during pregnancy and the doses of the drugs used are important.[7] Maternal AEDs therapy is often continued during pregnancy to avoid maternal and fetal risks associated with seizures. However, there is an increased risk of congenital malformation and negative cognitive development of AEDs, and these drugs should be well-monitored.[8,9]

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Hamilelik ve Epilepsi: Epilepsili Hamile Kadınların Klinik Verileri ve Olumsuz Sonuçları

Öz

Amaç: Epilepsili kadınlarda gebelik, konjenital malformasyonlar gibi fetal gelişim komplikasyonları açısından daha yüksek risk taşır. Bu çalışmada, üçüncü basamak epilepsi merkezindeki gebe epilepsi hastalarından elde edilen veriler sunulmuştur.

Gereç ve Yöntem: Çalışmamızda, Nisan 2011-Nisan 2021 tarihleri arasında epilepsi polikliniğinde takip edilen 110 gebeye ait 128 gebelik incelendi. Hastaların demografik verileri, kullanılan antiepileptik ilaçlar ve gebelik sonuçları geriye dönük olarak incelendi.

Bulgular: Gebelik sırasında 101 hasta (%78.9) monoterapi almış olup lamotrijin monoterapide en sık kullanılan ilaçtı. On sekiz hastada (%14.1) iki ilaç kombinasyonu, beş hastada (%3.9) üç ilaç kombinasyonu kullanıldı. Çoğu hastada nöbet sıklığı artmazken, 18 hastada (%14.1) nöbet sıklığı arttı, beş hastada ise (%3.9) azaldı. Çalışmamızda beş hastada intrauterin fetal kayıp, üç hastada konjenital malformasyonlu yenidoğan bebek ve bir hastada doğum sırasında neonatal ölüm meydana geldi. Çok değişkenli lojistik regresyonda kullanılan antiepileptik ilaçların sayısı, intrauterin fetal kayıp, neonatal ölüm ve konjenital malformasyonlu yenidoğanlar gibi olumsuz sonuçları öngördü.

Sonuç: Epilepsili gebe hastaların yönetimi hem anne hem de fetüs için zordur. Çalışmamızda kombinasyon tedavisi fetüs ve yenidoğan için olumsuz sonuçlarla daha fazla ilişkiliydi. Gebelik planlı olmalı ve düşük doz monoterapi ile nöbetsiz gebelik hedeflenmelidir.

Anahtar sözcükler: Antiepileptik ilaçlar; epilepsi; fetal malformasyon; gebelik.

In this study, the clinical data of pregnant women with epilepsy were analyzed retrospectively, and we aimed to present the results of adverse outcomes during pregnancy. Our study is one of the studies that evaluated the clinical follow-up and results of the highest number of pregnant patients with epilepsy in our country.

Materials and Methods

Data of 110 pregnant women with epilepsy and 128 pregnancies followed in the epilepsy outpatient clinic of Health Sciences University Prof. Dr. Mazhar Osman Psychiatric and Neurological Diseases Training and Research Hospital were included in the study. Patients between April 2011 and April 2021 were screened retrospectively, and their demographic data and pregnancy outcomes were evaluated. Gestational age, age at onset of epilepsy, duration of epilepsy, education level of patients, family history of pregnant women with epilepsy, and imaging results were recorded as demographic characteristics. AEDs used during pregnancy, and their doses were recorded. Pregnancy data, seizure frequency, and adverse outcomes were evaluated.

In our study, intrauterine fetal loss, neonatal death, and newborn congenital malformations were considered as adverse outcomes. Intrauterine fetal loss was defined as abortion for fetal deaths before 20 weeks and intrauterine fetal death for deaths after 20 weeks.

Pregnant patients with epilepsy between the ages of 18–40 were included in the study. Patients with insufficient data and follow-up were excluded as exclusion criteria. Ethics committee approval was obtained for the study (number: 2021-247).

Statistical analysis– All statistical analyses were performed using SPSS statistical software, version 19.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Previous history of abortion, the number of drugs used, and folic acid use during pregnancy were evaluated in univariate analysis for adverse outcomes in pregnancy (variables with $p<0.2$ in univariate analysis were considered significant). For multivariate analysis, these possible factors identified by univariate analysis were entered into logistic regression analysis for the independent predictor for adverse outcomes. $P<0.05$ was considered statistically significant.

Results

A total of 128 pregnancies of 110 epilepsy patients with a mean gestational age of 28.3±4.83 (18–40 years) were included in the study. The demographic characteristics, epilepsy types, and imaging results of the patients are shown in detail in Table 1.

Pregnancy data and adverse outcomes are shown in Table 2. Most of the patients were delivered by cesarean section. Although the frequency of seizures did not increase in most patients, the frequency of seizures increased in 18 patients (14.1%) and decreased in 5 patients (3.9%). Status epilepticus was not reported at the time of delivery, but two patients had epilepsy attacks. In our study, intrauterine fetal abortion occurred in four patients, intrauterine fetal death in one patient, newborn with a congenital malformation in three patients, and neonatal death during delivery in one patient. Of these nine patients, three were receiving two-drug combinations, two were receiving three-drug combinations, and four were receiving monotherapy. The drugs and doses used in these patients are shown in Table 2.

During pregnancy, 101 patients (78.9%) received monotherapy, and lamotrigine was the most commonly used drug in monotherapy. A two-drug combination was used in 18 patients (14.1%), and a three-drug combination was used in 5 patients (3.9%). AEDs used during pregnancy are shown in Table 3.

Table 1. Demographic characteristics of patients (n=110)

Gestational age	28.3±4.83 (18–40)
Age of onset of epilepsy (years)	16.6±6.0
Epilepsy duration (years)	13.6±7.4
Smoking patient	6 (5.5)
Patients who drink alcohol	2 (1.8)
Education level of the patients	
Illiterate	1 (0.9)
Primary education	54 (49.1)
High school	33 (30)
University	22 (20)
Family history of epilepsy	
No family history	67 (60.9)
First degree relative	15 (13.6)
Second degree relative	18 (16.4)
Third degree relative	10 (9.1)
Family history of congenital malformations	
No	107 (97.3)
Skeletal and muscular system	1 (0.9)
Central nervous system	1 (0.9)
Mental motor retardation	1 (0.9)
Patients whose parents are consanguineous	13 (11.8)
Epilepsy type	
Generalized	74 (67.3)
Partial	32 (29.1)
Unclassified	4 (3.6)
Cranial CT and MRI findings	
Normal	92 (83.6)
Mesial temporal sclerosis	3 (2.7)
Infarct	1 (0.9)
Encephalomalacia	3 (2.7)
Meningioma	1 (0.9)
Chiari malformation	1 (0.9)
Arachnoid cyst	1 (0.9)
Cavernoma	1 (0.9)
Corpus callosum agenesis	2 (1.8)
Porencephaly	2 (1.8)
Hypoxic changes	1 (0.9)
Other	2 (1.8)

Mean values (standard deviation) and n (%) were reported for continuous and categorical variables, respectively.

Table 2. Pregnancy data and adverse outcomes

Baby height (cm)	49.97±2.76
Baby weight (g)	3276±582
Baby head circumference (cm)	34.85±1.9
Pregnancy	
Single	127
Twin	1
Type of delivery (123 patients who gave birth)	
Normal delivery	52 (42.2)
Cesarean section	71 (57.8)
Time of birth (123 patients who gave birth)	
On time birth	109 (89.3)
Pre-mature birth	12 (9.8)
Post-mature birth	2 (1.6)
Patients' previous history of abortion	
No	92 (83.6)
Yes	18 (16.4)
Planned pregnancy	
Yes	86 (67.2)
No	42 (32.8)
Infertility treatment for pregnancy	
No	124 (96.9)
Yes	4 (3.1)
Frequency of seizures during pregnancy	
No seizure	50 (39.1)
Seizure frequency is the same	55 (43)
Seizure frequency increased	18 (14.1)
Seizure frequency decreased	5 (3.9)
Folic acid intake during pregnancy	
Yes	90 (70.3)
No	38 (29.7)

Adverse outcomes in pregnancy (fetus loss and malformed baby)	Drugs used
1. The mother is healthy, the baby is born ex, cesarean delivery	Lamotrigine (300 mg)
2. The mother is healthy, intrauterine abortion	Valproic acid (500 mg)+Levetiracetam (500 mg)
3. The mother is healthy, intrauterine abortion	Lamotrigine (400 mg)+Levetiracetam (1000 mg)
4. The mother is healthy, intrauterine fetus death, malformed fetus	Lamotrigine (400 mg) Levetiracetam (1000 mg)
5. The mother is healthy, intrauterine abortion	Carbamazepine (400 mg)
6. The mother is healthy, intrauterine abortion	Carbamazepine (400 mg)+Lamotrigine (400 mg)+Levetiracetam (3000 mg)
7. The mother is healthy, inguinal hernia in the baby, cesarean delivery	Valproic acid (750 mg)+Levetiracetam (2000 mg)
8. The mother is healthy, the baby has ventricular septal defect, normal delivery	Valproic acid (250 mg)+Levetiracetam (1500 mg)+Carbamazepine (1200 mg)
9. The mother is healthy, the baby has ventricular septal defect, normal delivery	Mean values (standard deviation) and n (%) were reported for continuous and categorical variables, respectively

Mean values (standard deviation) and n (%) were reported for continuous and categorical variables, respectively.

Table 3. Antiepileptic drugs used during pregnancy (n=128)

Number of drugs	Drug names	n (%)
Patients not taking medication	–	4 (3.1)
Patients taking a single drug		101 (78.9)
	Valproic acid	14 (10.9)
	Carbamazepine	25 (19.5)
	Lamotrigine	41 (32)
	Levetiracetam	18 (14.1)
	Topiramate	1 (0.8)
	Oxcarbazepine	2 (1.6)
Patients taking two drugs		18 (14.1)
	Lamotrigine-Levetiracetam	5 (3.9)
	Valproic acid-Levetiracetam	3 (2.3)
	Lamotrigine-Carbamazepine	2 (1.6)
	Carbamazepine-Levetiracetam	1 (0.8)
	Oxcarbazepine-Levetiracetam	3 (2.3)
	Lamotrigine-Topiramate	2 (1.6)
	Lamotrigine-Oxcarbazepine	2 (1.6)
Patients taking three or more drugs		5 (3.9)
	Valproic acid-Carbamazepine-Levetiracetam	1 (0.8)
	Valproic acid-Levetiracetam-Lamotrigine	1 (0.8)
	Levetiracetam-Topiramate-Valproic acid	1 (0.8)
	Carbamazepine-Zonisamide-Topiramate	1 (0.8)
	Carbamazepine-Levetiracetam-Lamotrigine	1 (0.8)

Mean values (standard deviation) and n (%) were reported for continuous and categorical variables, respectively.

Table 4. Parameters predicting adverse outcomes such as intrauterine loss and newborn death and newborn congenital malformations

	Univariate			Multivariate		
	OR	CI	P	OR	CI	P
Number of antiepileptic drugs used	1.021–69.43	2.66	0.045	2.81	1.007–7.884	0.049
History of abortion in previous pregnancy	0.684–13.152	3.00	0.145	3.02	2.28–14.9	0.166
Folic acid intake during pregnancy	0.625–9.867	2.48	0.196	2.72	0.635–11.672	0.178

OR: Odds ratio; CI: Confidence interval.

Parameters predicting adverse outcomes such as intrauterine fetal loss (fetal abortion and intrauterine fetal death), neonatal death, and newborn with congenital malformations are shown in Table 4. When the number of AEDs used during pregnancy, previous abortion, and folic acid use during pregnancy were entered into a multivariate logistic regression, only the number of AEDs used predicted adverse outcomes.

Discussion

In this study, pregnancy data of patients with epilepsy were evaluated. The number of AEDs used in multivariate logistic regression predicted adverse outcomes such as intrauterine fetal loss, neonatal death, and newborns with congenital malformations. While the frequency of seizures did not increase in most patients, the frequency of seizures increased in 18 patients (14.1%) and decreased in 5 patients (3.9%). Most patients were treated with monotherapy.

Women with epilepsy should continue the drug during pregnancy; otherwise, the risk of seizures in mother increases in case of discontinuation of the drug, adversely affecting the health of mother and baby.[10] It is important which AED is safer during pregnancy. In studies, valproate, phenobarbi-

tal, and topiramate were reported to have higher risk, while lamotrigine, levetiracetam, and oxcarbazepine were less risky in pregnancy. Doses of drugs used are as important as drug selection. It is known that the risk of malformation increases with drug doses.[11,12] Pharmacokinetic interactions of drugs on each other are important in the combination of AEDs; they can increase or decrease the effects of each other. In our study, most of the patients received monotherapy, and lamotrigine was mostly used in monotherapy. In studies, it is recommended to avoid combinations of levetiracetam + valproate; and levetiracetam + carbamazepine. It has also been reported that the combination of levetiracetam and lamotrigine is relatively less risky; we used this combination more in our study.[13,14] We found that combination therapy with carbamazepine or valproic acid was associated with adverse outcomes.

Pregnancy is associated with hemodilution, altered liver metabolism, and altered renal clearance. There may be changes in the gastrointestinal absorption and plasma protein binding of the AEDs. Therefore, it requires frequent adjustments in the dose of the AEDs every 3 months. Closer monitoring is required for lamotrigine, levetiracetam, oxcarbazepine, phenytoin, and topiramate. This intensive monitoring goes a long way in maintaining a seizure-free prenatal period without dose-related complications. The risk of seizures is maximum during labor and delivery. Fortunately, status epilepticus can occur in less than 1% of patients. Women with focal epilepsy, women receiving polytherapy, and women who had a seizure 1 month before pregnancy are at higher risk for increased seizures during pregnancy. [15] In our study, status epilepticus did not develop during delivery, but epileptic attacks occurred in two patients.

In a series of 55 diseases related to pregnant women with epilepsy in our country, it was found that the seizure frequency of 56.4% of the patients did not change, and the frequency of seizures increased in 21.8% of them. About 3.6% of the babies died in intrauterine period. Malformation was detected in 7.3% of the babies.[16] In a retrospective study involving 117 pregnant patients, major anomalies were found in 5.3% of the patients who received monotherapy, 20% of those who received multiple treatments, and 3.8% of the pregnant women with epilepsy who were followed up without medication.[17] In another study evaluating 87 pregnancies with epilepsy in our country, abortion was found in six patients, and congenital malformation was found in four patients.[18] In a study of 82 patients based in Brazil, women with resistant epilepsy noted that a significant risk of obstetric and neurological complications might arise. In this study, obstetric complications were significantly associated with polytherapy, multiple comorbidities, non-adherence to treatment, and worsening of seizures during pregnancy.[19]

Folic acid is essential in developing the central nervous system, especially in the first trimester of pregnancy, where rapid cell division occurs. The incidence of serious risks such as low birth weight, premature birth, and neural tube defect increases in the babies of pregnant women with folic acid deficiency. Pregnancy should be planned, and the most effective drug should be used at the lowest possible dose, and precautions such as folic acid should be taken.[20] According to the European and International Registry of Antiepileptic Medicines and Pregnancy, while it is important to target the lowest effective dose of AEDs during conception and early pregnancy, dose adjustment should be considered as pregnancy progresses.[21]

Although there is no change in seizure frequency during pregnancy in most women with epilepsy, epileptic seizures may increase in about 1/3 of them. During pregnancy, estrogen and progesterone can change neuronal excitability and seizure threshold.[22] In our study, an increase in seizure frequency was observed in 14.1% of our patients.

The patients with epilepsy had a previous history of abortion during pregnancy, the number of AEDs and the use of folic acid were evaluated in the univariate analysis. Among these parameters, it was observed that adverse outcomes increased in the multivariate analysis as the number of AEDs used increased. The rates of intrauterine loss and neonatal birth with malformation were higher in patients receiving combined treatment with carbamazepine and valproic acid than in patients receiving monotherapy.

Limitations of the study– The first limitation is that it is a single-center study, and the number of patients is limited. Second, the limitations of the retrospective study are present in our study. The changes in drugs and doses were not detailed in the study.

Conclusion– While using AEDs, the side effects of these drugs on the fetus should be considered, and appropriate drugs should be selected that will provide maternal stabilization and control seizures. Combination therapy during pregnancy is associated with adverse outcomes. Pregnancy should be planned, and seizure-free pregnancy should be targeted with low-dose monotherapy.

Informed Consent– Due to the retrospective design of the study, informed consent was not taken.

Ethics Committee Approval– This study approved by the Bakirkoy Dr. Sadi Konuk Training and Research Hospital Eth-

ics Committee (Date: 19.04.2021, Number: 2021-247).

Peer-review– Externally peer-reviewed.

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References

1. Gul ZB, Atakli HD. Effect of the COVID-19 pandemic on drug compliance and stigmatization in patients with epilepsy. Epilepsy Behav 2021;114:107610. [CrossRef]
2. Gul ZB, Celik RG, Yilmaz MU, Aksoy S, Teker SR, Mutluer BT, et al. The ımpact of the Coronavirus disease 2019 outbreak on the quality of life of patients with epilepsy. Epilepsi 2021;27(2):78–84.
3. Thomas SV. Management of epilepsy and pregnancy. J Postgrad Med 2006;52(1):57–64.
4. Mawer G, Briggs M, Baker GA, Bromley R, Coyle H, Eatock J, et al. Pregnancy with epilepsy: Obstetric and neonatal outcomeof a controlled study. Seizure 2010;19(2):112–9. [CrossRef]
5. Thomas SV, Sindhu K, Ajaykumar B, Devi PB, Sujamol J. Maternaland obstetric outcome ofwomen with epilepsy. Seizure 2009;18(3):163–6. [CrossRef]
6. Nie Q, Su B, Wei J. Neurological teratogenic effects of antiepileptic drugs during pregnancy. Exp Ther Med 2016;12(4):2400–4. [CrossRef]
7. Tekin B. Epilepsy, pregnancy, and antiepileptic drugs. Epilepsi 2018;24 Suppl 1:41–3.
8. Tomson T, Battino D. Teratogenic effects of antiepileptic drugs. Lancet Neurol 2012;11(9):803–13. [CrossRef]
9. Razaz N, Tomson T, Wikström AK, Cnattingius S. Association between pregnancy and perinatal outcomes among women with epilepsy. JAMA Neurol 2017;74(8):983–91. [CrossRef]
10. Meador KJ. Epilepsy: Pregnancy in women with epilepsy-risks and management. Nat Rev Neurol 2014;10(11):614–6. [CrossRef]
11. Vajda FJ, Hitchcock A, Graham J, O'Brien T, Lander C, Eadie M. Seizure control in antiepileptic drug-treated pregnancy. Epilepsia 2008;49(1):172–6. [CrossRef]
12. Borgelt LM, Hart FM, Bainbridge JL. Epilepsy during pregnancy: Focus on management strategies. Int J Womens Health 2016;8:505–17. [CrossRef]
13. Pennell PB. Use of antiepileptic drugs during pregnancy: Evolving concepts. Neurotherapeutics 2016;13(4):811–20. [CrossRef]
14. Veroniki AA, Cogo E, Rios P, Straus SE, Finkelstein Y, Kealey R, et al. Comparative safety of anti-epileptic drugs during pregnancy: A systematic review and network meta-analysis of congenital malformations and prenatal outcomes. BMC Med 2017;15(1):95. [CrossRef]
15. Cagnetti C, Lattanzi S, Foschi N, Provinciali L, Silvestrini M. Seizure course during pregnancy in catamenial epilepsy. Neurology 2014;8(4):339–44. [CrossRef]
16. Pak AT, Bozdemir H, Aslan K, Peköz T, Büyükkurt S, Ünal İ. Prevalence of seizures in pregnant women with epilepsy and pregnancy outcomes. Epilepsi 2018;24(3):114–9.
17. Güveli BT, Rosti RO, Güzeltaş A, Tuna EB, Ataklı D, Sencer S, et al. Teratogenicity of antiepileptic drugs. Clin Psychopharmacol Neurosci 2017;15(1):19–27. [CrossRef]
18. Kutlu G, Erdal A, Aydoğan S, Gomceli YB, İnan LE. Follow up and treatment of women with epilepsy during pregnancy. J Neurol Sci 2012;29(3):527–34.
19. Vitturi BK, Cabral FB, Cukiert CM. Outcomes of pregnant women with refractory epilepsy. Seizure 2019;69:251–7. [CrossRef]
20. Kjaer D, Horvath-Puhó E, Christensen J, Vestergaard M, Czeizel AE, Sørensen HT, et al. Antiepileptic drug use, folic acid supplementation, and congenital abnormalities: A population-based case-control study. BJOG 2008;115(1):98–103. [CrossRef]
21. Battino D, Tomson T, Bonizzoni E, Craig J, Lindhout D, Sabers A, et al. Seizure control and treatment changes in pregnancy: Observations from the EURAP epilepsy pregnancy registry. Epilepsia 2013;54:1621–7. [CrossRef]
22. Harden CL, Meador KJ, Pennell PB, Hauser WA, Gronseth GS, French JA, et al. Practice parameter update: Management issues for women with epilepsy-focus on pregnancy (an evidence-based review): Teratogenesis and perinatal outcomes: Report of the quality standards subcommittee and therapeutics and technology assessment subcommittee of the American academy of neurology and American epilepsy society. Neurology 2009;73(2):133–41. [CrossRef]