

The Clinical Characteristics of Epileptic Pregnant Women

Mahmut ERDEMOĞLU, Umur KUYUMCUOĞLU, Ali İrfan GÜZEL

Diyarbakır, Turkey

OBJECTIVE: We aimed to report the clinical characteristics 16 pregnant epileptic women applied to our clinic.

STUDY DESIGN: The data were collected from the hospital records and patient files retrospectively.

RESULTS: Our study indicates that the rate of complications of pregnancy in mothers with active epilepsy is low and similar to that of the general population with epilepsy. There were no maternal or perinatal deaths.

CONCLUSION: It is concluded that epileptic women may expect good maternal and fetal outcome with qualified prenatal medical and obstetric care.

Key Words: Epilepsy, Pregnancy, Pregnancy outcomes

Gynecol Obstet Reprod Med; 2010;16:152-5

Introduction

About 40% of 18 million females with epilepsy in the world are in the reproductive age group. Pregnant epileptic women (PEW) are perceived to have increased risk of complications during pregnancy and delivery. PEW tends to marry late, and have fewer children than women without epilepsy.¹ PEW may have increased risk of spontaneous abortion, non-proteinuric hypertension, antepartum hemorrhage, toxemia, induction of labor and caesarian section when compared to general population.^{2,3} Some epileptic women may experience seizure only during pregnancy which is termed gestational epilepsy; such women would be seizure free between pregnancies. Another subgroup (Gestational onset Epilepsy) may have their first seizure during pregnancy and thereafter may continue to get spontaneous recurrent seizures.⁴ In recent studies,⁵ including 2385 pregnancies found increased seizure frequency in 35%, decreased frequency in 15% and no change in 50%. The more frequent the seizures before conception, the more likely do these increase in frequency during pregnancy. Seizure exacerbation may occur at any time, but is most frequently encountered at the end of the first and at the beginning of the second trimester.⁶ Optimizing pregnancy outcome and

counseling of the patients with epilepsy will still require an increased knowledge of specific risk factors.

The objective of this study is to retrospectively ascertain the maternal and fetal outcomes of PWE applied to our clinic.

Material and Method

The study included all women with epilepsy who had given birth at the Department of Obstetrics and Gynecology, Dicle University School of Medicine, during January 2008-December 2008. Data were collected retrospectively. The gynecological and obstetric past history and family history were recorded. The demographic characteristics, maternal age, delivery modes, neonatal weight, Apgar scores, cesarean rates and indications, fetal anomalies, perinatal mortality rates how many years they had epilepsy, the last time of their seizure and the epileptic drugs they used before pregnancy were evaluated. (Table 1) The fetuses evaluated for major congenital anomalies by 4D ultrasound examination (Voluson 730 PRO) at 18-22 weeks of pregnancy. All of the cases were evaluated and the neurological examination was made by a neurologist. Epilepsy was not considered an indication for induction of labor. During labor and delivery, the epileptic women were treated according to the general obstetric principles.

Results

From January 2008 and December 2008, there were 16 (0.59%) complicated pregnancies with epilepsy and these cases have been evaluated retrospectively. All of the cases recalled receiving preconceptional counseling. During this period there were 2676 births. The mean age of the cases were 25.50 (18-40), the mean gravidity was 2.18 (1-6) and mean par-

Dicle University School of Medicine Department of Obstetrics and Gynecology, Diyarbakır

Address of Correspondence: Ali İrfan Güzel
Dicle University School of Medicine
Department of Obstetrics and
Gynecology, Diyarbakır
alijnk@hotmail.com

Submitted for Publication: 22. 07. 2010

Accepted for Publication: 25. 10. 2010

ity was 0.93 (0-5). The mean gestational weeks of the cases were 37.62 weeks (36-40 week). 12 (75%) of the fetuses were in vertex and 4 (25%) were in breech presentation. 15 (93.75%) of the epileptic cases were diagnosed before their pregnancy. One of the cases applied to our clinic with tonic clonic seizures and on electroencephalographic examination she took epilepsy diagnosis for the first time. 13 (81.25%) of the cases were using carbamazepine and 3 (18.75%) were using sodium valproate during their pregnancy. Both of these drugs are fetotoxic when used during pregnancy. Carbamazepine is in category C and sodium valproate is D. The cases had not any seizures during their pregnancy. We have consulted the all cases with neurology department before delivery. 4 (25%) of the cases delivered by cesarean section, 12 (75%) cases delivered by spontaneous vaginal route. After delivery, babies examined and there was not any anomaly with related antiepilep-

tic drugs. All of the cases discharged from the hospital with refer to the neurology clinic for routine neurologic follow up.

Discussion

Epilepsy is the second frequent neurological disorder after migraine during pregnancy. Seizures can occur during pregnancy or immediate postpartum period due to several causes. Seizures due to eclampsia, central nervous system infections, cerebral venous sinus thrombosis, and other acute medical conditions are grouped under special syndromes in the classification of epileptic syndromes according to the International League Against Epilepsy.⁷ Most seizures during pregnancy occur in women who already have epilepsy. During pregnancy most women will continue their previous level of seizure control, although 15-30% may experience an increase

Table 1: The clinical characteristics of the cases

Cases	Age	Gravidity	Parity	Gest. Week	Presentation	Time of epilepsy diagnosis	Antiepileptic drug using period during pregnancy (month)	Complication	Fetal anomaly	Delivery	Fetal weight(g)/Apgar (1-5 minute)
1	29	1	0	37	Vertex	At our clinic	Carbamazepine	-	-	Spontaneous vaginal delivery	3000/6-8
2	22	3	1	36	Vertex	8 years	Carbamazepine	-	-	Spontaneous vaginal delivery	2900/5-7
3	26	4	3	38	Vertex	10 years	Carbamazepine	-	-	Spontaneous vaginal delivery	3450/7-9
4	21	1	0	37	Vertex	11 years	Sodium valproate	-	-	Spontaneous vaginal delivery	3100/5-7
5	19	1	0	37	Breech	12 years	Sodium valproate	-	-	Cesarean section	2990/4-8
6	20	1	0	38	Vertex	10 years	Carbamazepine	-	-	Spontaneous vaginal delivery	3400/6-9
7	25	3	2	39	Vertex	7 years	Carbamazepine	-	-	Spontaneous vaginal delivery	3600/5-9
8	22	1	0	37	Vertex	12 years	Carbamazepine	-	-	Spontaneous vaginal delivery	2880/6-8
9	33	3	2	40	Breech	20 years	Carbamazepine	-	-	Cesarean section	3700/7-9
10	25	1	0	37	Vertex	3 years	Carbamazepine	-	-	Spontaneous vaginal delivery	3120/6-8
11	24	1	0	38	Breech	12 years	Carbamazepine	-	-	Cesarean section	3400/5-7
12	40	6	4	37	Vertex	11 years	Carbamazepine	-	-	Spontaneous vaginal delivery	3140/5-9
13	37	4	2	36	Vertex	6 years	Sodium valproate	-	-	Spontaneous vaginal delivery	2800/4-7
14	25	3	1	39	Vertex	12 years	Carbamazepine	-	-	Spontaneous vaginal delivery	3560/5-7
15	22	1	0	37	Vertex	11 years	Carbamazepine	-	-	Spontaneous vaginal delivery	2900/4-8
16	18	1	0	39	Breech	8 years	Carbamazepine	-	-	Cesarean section	3500/6-9

in seizures.⁸ Similarly, seizure frequency remained unchanged (63.6%) or abated (15.9%) in most of the PEW according to another recent multinational prospective study.⁹ The incidence of seizure did not increase in our 16 cases. Thomas et al, indicate that most epileptic women have uneventful pregnancy and delivery.¹⁰ There is an increased risk of spontaneous abortion, pregnancy induced hypertension, pre-eclampsia, anemia, and peripartum seizures as compared to women without epilepsy attending to a large teaching hospital. A prospective study of pregnancies in Northern Region of United Kingdom, through community midwives and review of medical records had shown that epileptic women (compared to background population) did not have any excess risk of complications of pregnancy except for premature labor.¹¹ There were not such complications of the cases in our study. In an Iceland study, the cesarean rate was twice and incidence of breech presentation was 5% in PEW.¹² The cesarean and breech presentation rate was not increased in our study. Mullers-Kuppers first described the association between prenatal exposure to antiepileptic drugs and major congenital malformations. He reported a boy with microcephalus and cleft palate born to a mother taking mephenytoin for epilepsy.¹³ Controlling seizures during pregnancy is vital, as seizures are likely to have an adverse effect on the developing fetus. Generalized tonic-clonic seizures might cause hypoxia, leading to damage of the CNS as well as of other organ systems, and sustained hypoxia can result in fetal death. In a study of pregnant rats, induction of seizures resulted in neuronal damage in numerous regions of the fetal CNS, including the hippocampus.¹⁴ The conventional drugs i.e. phenytoin, carbamazepine, phenobarbital, valproate are all appropriate in pregnancy. The main practical issue is the teratogenicity of these drugs. In general, the risk of congenital defects is low - 2-3% in overall population of pregnant women which increases to 4-5% in women taking anticonvulsants.¹⁵ Olafsson et al, reported that risk major of congenital anomaly is increased almost threefold when the PEW treated with anti epileptic drugs, the risk is highest with sulthiame and lowest with carbamazepine.¹² A population-based study of over 20,000 patients with epilepsy identified 939 births among 561 untreated patients and 1,411 births among 857 patients using antiepileptic drugs in the first trimester.¹⁶ In this study, valproate was associated with increased risk of congenital malformations compared with the offspring of untreated patients. The risk of congenital malformations did not increase in the offspring of mothers using carbamazepine, oxcarbazepine or phenytoin (as monotherapy or polytherapy without valproate). We did not detect any congenital anomaly in our cases.

In conclusion, optimal seizure control is achieved prior to conception and that monotherapy with the lowest effective dosage be employed. With qualified prenatal medical and obstetric care, the great majority of women with epilepsy can be

assured of an uncomplicated pregnancy and of normal healthy offsprings.

Epilepsili Gebe Kadınların Klinik Özellikleri

AMAÇ: Kliniğimize başvuran 16 epilepsili gebe kadının klinik karakteristiklerinin sunulması amaçlanmıştır.

GEREÇ VE YÖNTEM: Veriler retrospektif olarak hastane kayıtlarında ve hasta dosyalarında kaydedilmiştir.

BULGULAR: Bizim çalışmamız aktif epilepsisi olan gebe kadınlardaki komplikasyon oranının düşük olduğunu ve epilepsisi olan genel popülasyonla benzer olduğunu öngörmektedir. Maternal ve perinatal ölüm gerçekleşmemiştir.

SONUÇ: Epilepsili kadınlarda kaliteli prenatal takip ve obstetrik bakım ile iyi maternal ve fetal sonuçlar alınabileceği sonucuna varılmıştır.

Anahtar Kelimeler: Epilepsi, Gebelik, Gebelik Sonuçları

References

1. Thomas SV, Deetha TD, Kurup JR, Reghunath B, Radhakrishnan K, Sarma PS. Pregnancy among women with epilepsy. *Ann Indian Acad Neurol* 1999;2:123-8.
2. Richmond JR, Krishnamoorthy P, Andermann E, Benjamin A. Epilepsy and pregnancy: an obstetric perspective. *Am J Obstet Gynecol* 2004;190:371-9.
3. Nelson KB, Ellenberg JH. Maternal seizure disorder, outcome of pregnancy, and neurologic abnormalities in the children. *Neurology* 1982;32:1247-54.
4. Commission on classification & terminology of International League against epilepsy 1989 proposal for revised clarification of epilepsies and epileptic syndromes *Epilepsia* 1989;30:389-99.
5. Hollingsworth DR, Resnik R. Medical counselling before pregnancy. New York, Churchill Livingstone, 1988, pp 415.
6. Browne T R, Gregory L, Holmes G L, Montouris G D. Special considerations in Women. In: Browne T R, Holmes G L (eds), *Handbook of Epilepsy*, 3rd edition. Lippincott Williams & Wilkins, 2004 pp. 216.
7. Commission on classification and terminology of the International League Against Epilepsy, 1989;30:389-99.
8. Beach RL, Kaplan PW. Seizures in pregnancy: diagnosis and management. *Int Rev Neurobiol.* 2008;83:259-71.
9. Seizure control and treatment in pregnancy: observations from the EURAP epilepsy pregnancy registry. EURAP Study Group. *Neurology* 2006;66:354-60.
10. Thomas SV, Sindhu K, Ajaykumar B, Sulekha DPB, Sujamol J. Maternal and obstetric outcome of women with epilepsy. *Seizure* 2009;18:163-9.

11. Fairgrieve SD, Jackson M, Jonas P, Walshaw D, White K, Montgomery TL, et al. A Lynch Population based prospective study of the care of women with epilepsy in pregnancy. *BMJ* 2000;321:674-5.
12. Olafsson E, Hallgrimsson JT, Hauser WA, Ludvigsson P, Gudmundsson G. Pregnancies of women with epilepsy: a population-based study in Iceland. *Epilepsia* 1998;39:887-92.
13. Hernandez-Diaz S, Werler MM, Walker AM, et al. Folic acid antagonists during pregnancy and the risk of birth defects. *N Engl J Med* 2000;30:1608-14.
14. Hallak M et al. Fetal rat brain damage caused by maternal seizure activity: prevention by magnesium sulfate. *Am J Obstet Gynecol* 1999;181: 828-34.
15. Ropper Allan H, Brown Robert H. Epilepsy and other seizures disorders. *Adam's and Victor's Principles of Neurology*, 8th edition. McGraw Hill, 2005, pp 296.
16. Lindhout D et al. Antiepileptic drugs and teratogenesis in two consecutive cohorts: changes in prescription policy paralleled by changes in pattern of malformations. *Neurology* 1992; 42: 94-110.