ANTICONVULSANT DRUGS AND WOMEN WITH SEIZURES

B.RAMAMURTHI • MANJULA DUTTA • KANTHIMATHI DAVID

ABSTRACT

The incidence of congenital anomalies in children born to mothers under anticonvulsant therapy has been studied, in 2536 women who gave birth to 3348 children. The follow up period varied between 3 to 20 years. The mothers had received barbiturates, hydantoinates and carbamezapine in various combinations. The incidence of congenital anomalies noted was only 41, a figure not greater than the incidence ofanomalies in the general population. A plea is made that anticonvulsant therapy should not be discontinued during pregnancy in women with seizures.

INTRODUCTION

Women suffering from seizures become concerned at the onset of pregnancy, about the control of seizures, the proper development of the foetus and possible complications during the course of the pregnancy and delivery. Should they start a pregnancy ? If one has occured, should they continue it ? Do seizures increase in pregnancy and will the development of the foetus be affected ? Worldwide experience in the management of epileptic women with pregnancy has shown that most of these anxieties are misplaced and with proper counselling and adequate therapy, pregnancy and childbirth could be smooth without any problems.

One fact to be stressed is that proper seizure control is essential throughout. This emphasis has become necessary as some obstetricians unfortunately advise stoppage of the drugs the moment they learn that the women is pregnant, based on the fear that all anticonvulsant drugs are teratogenic. If it is not the obstetrician, the husband and the in-laws insist on the stoppage resulting in serious problems. The problems that a young Indian woman faces under these circumstances is distressing.

Pregnancy is likely to cause an increase in seizures (Knight and Rhind 1975, Philbert and Dam 1982), but more often this is due to stoppage of the drugs or inadequate medication. (Schmidt and over 1983). Generalised seizures occuring during pregnancy can be hazardous to the mother and child and specially if status epilepticus develops. in a series of mothers with status epilepticus, nine mothers and 14 infants died (Teramo and Hillsema 1982). A single generalised

Dept. of Obst. & Gyn, Dr. A. Lakshmipathi Neurosurgical Centre Voluntary Health Services, Madras.

Acccepted Publication on 16/6/92.

convulsion may lead to a stillbirth (Higgins and Commerford 1974). When the seizures are poorly controlled, the complications of pregnancy are likely to increase (Teramo and Hillsema 1982, Yerby and Kopsell 1985).

Thus it is obvious that anticonvulsant drugs have to be continued throughout, but one would like to known how teratogenic are these drugs. In experimental animals these drugs were shown to be teratogenic; but in the humans in the required doses the evidence is not complete, though there are reports of increased incidence of abnormalities in treated mothers (Spiedel and Meadow, 1972). The Oxford Record Linkage Study reported seventy abnormalities in every 1000 births to epileptic mothers, two to four times the rate in the general population. (Fedrick 1973). Large doses of phenytoin may cause some develop mental syndromes in the infant (Hanson and Smith 1975). Trimethadione (no longer in use) and sodium valproate (Lindhurst and Schmidt 1986) have been proved to have definite teratogenie effects. But how frequent is the occurence of congenital defects in women on other anticonvulsant drugs :

A study of the possible teratogenicity of anticonvulsants in epileptic mothers would involve the following :

1. Proof that congenital malformations occur in a significantly greater percentage in women who are taking anticonvulsant drugs.

2. Proof that this increased incidence is due to the drugs and not due the epileptic characteristics itself or other factors like socioeconomic status, dietary deficiencies and obstetric factors like maternal age etc.

MATERIALS AND METHODS

An attempt has been made to study this problem by analysing the records of 3500 women who got married during their treatment for epilepsy, with a follow up period varying from 3 to 20 years. Of these, 2536 women had given birth to 3348 children. 1936 had one child, 388 had 212 had three children.

The drugs given were as follows :

Hydantoinates alone	150 patients
Hydantoinates and barbiturates	1630 patients
Barbiturates alone	215 patients
Hydantoinates and carbamezapine	246 patients
Carbameapine alone	340 patients

The number of congenital malformations seen in this group of 2536 women with 3348 children was only 41.

Table - I

Anticonvilsants and Congenital Malformation

1960 - 1986

Congenital Anomalies Seen

Total number of children	2865
Malformation seen at birth	5
Polydactyly	7
Talipes	8
Cardiovascular	5
Cleftlip	4
Meningomyelocele	3
Hydrocephalus	2
G.I. Tract	2
Others	5
Total	41

DISCUSSION

Studies conducted by the ICMR show that the rates of congenital malformations in the normal population vary between 18 - 32 per 1000.

The above studies show that the incidence of congenital malformations in the general population in India varies between 17 to 34 per thousand in different Parts of the country. Taking the

Table - II

Incidence of Congenital Malformations

Hospital based (live birth only)

		No. of births	Major malformation per 1000
Bombay	1966- 67	10,000	17.0
Bombay	1968 - 72	12,360	18.7
Pondicherry	1971- 72	3,46	21.0
Mean		8,595.3	18.9
Delhi	1969- 73	7,590	26.2
Ballabgarh	1976 - 77	2,409	34.1
Mean		4999.5	30.15

Table - III

Incidence of Congenital Malformation

Madras - M. S. Ramakrishnan Et Al

23000 consecutive births 1972 - 1974	(Hospital based)
Malformation children	18.9 per 1000 births
Incidence of malformations (including autopsy studies)	30.7 per 1000 births

lowest incidence of 17 per thousand, the incidence of congenital anomalies in the above series of 3348 children should have been 46. It is to be noted that the finding of 41 anomalies in treated mothers in our series is less than the expected average incidence in the general population. Thus this study does not confirm the observation of increased incidence of congenital anomalies in mothers taking anticonvulsants.

It has to be mentioned here that the women and children under this study belong to the middle economic group whereas the figures in table II and III are from the lower socioeconomic group. It is known that the socioeconomic status influences the incidence of these anomalies more of them occuring in the poorer groups. (Lawrence et al 1980).

CONCLUSIONS

Considering all the various aspects, one may suggest that sodium valproate should definitely be avoided during pregnancy and the best therapy may be with carbamezapine. Still there is a problem as this drug is costly and in India many

women of lower socioeconomic status may not be able to afford the high cost of continuous carbamezapine medicationand will have to continue on hydantoinates and perhaps barbiturates. The above study suggests that such a course need not cause undue anxiety to the women or to their obstetricians as the incidence of congenital anomalies with the usual doses of hydantaoinates and barbiturates does not seem to be higher that the incidence in the general population.

One may conclude that during pregnancy, to ensure safety of the mother and child, anticonvulsant drugs should be continued at adequate levels without any break; from our available knowledge, though carbamezapine would the best choice, hydantoinates and barbiturates may also be advised, when economics precludes a large expense on costly drugs.

REFERENCES

1. *Fedrick J., Brit, Med. J., 2 : 442, 1973.*
2. *Hanson J. W., Smith D.W., J. Paedia., 87 : 284, 1975.*
3. *Higgins TA., Commerford J. of the Irish Med. Assoc., 67 : 317, 1974.*
4. *Knight A.H., Rhind E.G., Epilepsia 16 : 99, 1975.*
5. *Lawrence K.M., N. James M., Miller M. and Campbell H., Brit. Med. J. 281: 1592, 1980.*
6. *Lindhurst D., Schmidt D., Lancet 1392 : 1986.*
8. *Philbert A., Dam M., Epilepsia 23 : 85, 1982.*
9. *Schmidt D, Conven R, J. Neurol, Neurosurg. Psych 4 6 : 75, 1983.*
10. *Spiedel B.D. and Meadow SR., Lancet 2 : 839, 1972.*
11. *Literature; In Janz D., Bossi M., Dam M., Et Al; E.D.S., Epilepsy, Pregnancy and the child New York, Raven Press, 53, 1982.*
12. *Yerby M.S., Kopsell T., Daling J.; Epilepsia, 26 : 631, 1985.*